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# BULLETIN of the JOHNS HOPKINS HOSPITAL

THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL
SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY

## August, 1943

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PUBLISHED MONTHLY

THE JOHNS HOPKINS PRESS, Baltimore-18, Maryland

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*This periodical is issued monthly.* Two volumes a year are issued, each consisting of approximately 400 pages, and beginning in January and July, respectively.

*Subscription price.* In the United States and its possessions $6.00 per year. In Canada $6.25 per year; in foreign countries $6.50 per year. Prices for back volumes and back single numbers on application. Single numbers of the current volume, when available, $.75. Prices are net, postpaid.

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THE JOHNS HOPKINS PRESS
BALTIMORE-18, MARYLAND, U. S. A.

Entered as second-class matter at the Baltimore, Md., Postoffice. Acceptance for mailing at special rate of postage provided for in Section 1103, act of October 3, 1917. Authorized on July 3 1918.

# A STUDY OF THALAMO-CORTICAL RELATIONS IN THE RABBIT

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Received for publication April 6, 1943

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## INTRODUCTION

Despite many investigations in which relations of thalamic nuclei to cerebral cortex have been studied in mammals by the method of secondary (retrograde) degeneration, two important questions still remain unsettled: What is the maximal extent of thalamic degeneration produced by removal of the whole cerebral cortex (neo-, paleo- and archicortex)? Which thalamic nuclei remain intact in such an experiment? This is so because removal of the entire cerebral cortex without injury to subcortical telencephalic centers is such a difficult procedure that no experiment yet reported has even approximately fulfilled the anatomical requirements. It is possible, however, to attack this problem indirectly. If one removes the whole telencephalon, *i.e.*, the whole cerebral cortex plus the subcortical telencephalic centers, then the thalamic nuclei which remain intact form a thalamic group which is completely independent of the cortex and, in fact, of the whole telencephalon. The degenerated nuclei, on the other hand, constitute telencephalic dependencies, which, in turn, may be composed of cortical dependencies and striatal dependencies, provided that the latter group really exists in the thalamus. Unfortunately, there are very few experiments of this sort in the literature.

For partial separation of cortical and possible striatal dependencies, another set of experiments is useful. If the subcortical telencephalic centers are left intact, while the whole cerebral cortex is removed, except for cortex directly adjacent to the subcortical ganglia, then the degenerated thalamic nuclei are cortical dependencies only; however, those nuclei, which remain unchanged in this experiment but degenerate after complete ablation of the telencephalon, may depend either on the cortex overlying the subcortical ganglia or on the subcortical ganglia themselves, or finally, on both.

In the following account we shall present results obtained on the rabbit with both types of experiment. It will be shown that after ablation of the whole telencephalon the behavior of the thalamic nuclei follows a rather simple pattern, highly consonant with ontogenetic and comparative anatomical considerations. It will be shown, further,

that the group of striatal dependencies must be very small if existent at all in the rabbit.

For the sake of clarity it is essential to define some concepts which will be used. It is rather general usage to infer, from secondary degeneration of a thalamic nucleus, the existence of a thalamo-cortical connection and to deny such a connection if the thalamic nucleus remains intact after ablation of the cortex. It is, of course, obvious that, if a thalamic nucleus does degenerate after destruction of a certain sector of the cortex, the existence of a thalamo-cortical connection can be assumed. If, however, a nucleus remains unchanged after removal of the cortex, this is important evidence but still not entirely conclusive that the nucleus lacks corticipetal connections. As a matter of fact, some thalamic nuclei which certainly remain unchanged after destruction of the whole cerebral cortex, nevertheless, are said by certain authorities to have some corticipetal connections. Therefore, we shall make use of the concept of von Monakow and refer to degenerated nuclei as "dependencies." We shall speak of telencephalic dependencies when it is uncertain whether the degenerated thalamic nuclei depend on cortex or on subcortical telencephalic centers, of cortical dependencies when they depend on cortex only, and, finally, of striatal dependencies when they depend on subcortical telencephalic centers. Theoretically, the latter group could be subdivided into amygdalar dependencies and striatal (n. caudatus and putamen) dependencies. Since, however, we are unable to prove that any degeneration in the thalamus is caused by destruction of all the subcortical telencephalic centers, we shall refer to this whole hypothetical group as striatal dependencies.

As cortex, we consider, with M. Rose (1926), all telencephalic structures which are stratified and possess at least two layers, of which the external is the zonal lamina. Thus all those structures described as cortical areas by M. Rose (1931) in his atlas of the rabbit, including nearly all the superficial structures of the so-called olfactory brain, are cortex. We do not agree with M. Rose in classing as cortex the septum pellucidum, because, in our opinion, it does not fulfill the conditions of the definition. Contrary to M. Rose, we regard the area diagonalis not as a cortical area but as a part of the hypothalamus (J. E. Rose, 1942a). By subcortical telencephalic centers we mean

n. amygdalae, n. caudatus and putamen. The latter two make up the striatum. The globus pallidus is believed to be a part of the hypothalamus (J. E. Rose, 1942a). The claustrum is considered an integral part of the insular cortex.

In speaking of cortical areas or regions, M. Rose's delimitations and nomenclature will be used unless otherwise stated. The nomenclature of the thalamic nuclei is essentially the same as that employed by one of us in a previous paper (J. E. Rose, 1942b).

## MATERIAL AND METHODS

The material on which this report is based consists of 8 brains. In some animals the whole telencephalon on one side was removed; in others the subcortical telencephalic centers were left intact but as much of the cortex as possible was removed unilaterally. In 2 specimens the goal of the operation was not that of removing one cortex, but the damage done was greater than intended so that these series were useful for this report. All operations were essentially unilateral. In some cases a small lesion purposely was placed in the other hemisphere or some damage was done unintentionally. The effects of these small lesions will be described separately in a report on the effects of small circumscribed cortical ablations.

Cortical tissue was removed with an aspiration technic now generally employed for cerebral operations in the Department of Physiology. By this method it is possible to control rather carefully the extent of an ablation and at the same time to minimize or avoid trauma to structures one wishes to leave intact. With correctly shaped glass aspirator tips of proper dimensions and with the right amount of negative pressure from the suction pump, all portions of the cortex may be separated from the underlying white matter, which, therefore, acts to protect subcortical structures. Care also permits one to remove tissue without severing the main blood vessels—a point which is of considerable importance for the control of bleeding, the maintenance of a clear operative field and the preservation of an adequate blood supply to remaining tissue. In certain respects use of this technic on the rabbit brain is more difficult than on the brains of carnivores and monkeys, but in our experience it is the best method for all experiments of this type.

Animals were sacrificed 18 to 28 days after operation. The brains were removed, fixed in alcohol, embedded in paraffin and cut at 20$\mu$ either in frontal or horizontal series. Every fourth section was stained with thionin for cells and usually every fifth for fibers by the Spielmeyer method.

## RESULTS

### *A. Changes in the thalamus following complete ablation of the telencephalon*

***Normal anatomy of the rabbit's thalamus.*** Before considering the experimental material some remarks on the normal anatomy of the

rabbit's thalamus are necessary. According to ontogenetic and comparative anatomical observations (J. E. Rose, 1942a, 1942b) we divide the thalamus of the rabbit into three main parts: (1) the epithalamus, (2) the dorsal thalamus, and (3) the ventral thalamus. The epithalamus of this classification includes the habenular complex, the paraventricular complex and the pretectal group of nuclei. The ventral thalamus consists of the reticular complex, the ventral lateral geniculate body and the rather indistinct suprahypothalamic group. In the dorsal thalamus we distinguish the anterior, the medial, the ventral, the dorsolateral, the midline and the intralaminar nuclear groups, the medial and the dorsal lateral geniculate bodies. The anterior group consists of n. anterodorsalis, n. anteroventralis and n. anteromedialis. The medial group contains n. parataenialis, n. mediodorsalis, n. medioventralis and the postmedial group, which includes n. parafascicularis and centrum medianum. In the ventral group n. ventroanterior, the ventrolateral complex and the ventrobasal complex are distinguished. The latter consists of at least two major elements—pars arcuata and pars medialis. Provisionally, we also place the magnocellular or angular nucleus of the rabbit in the ventral group. In the dorsolateral group we distinguish n. lateralis, n. posterior and the complex of the pulvinar. The midline structures and intralaminar nuclei present special difficulties. It has been suggested (J. E. Rose, 1942b) that nn. centralis medialis, rhomboidalis, centralis lateralis, paracentralis and interanteromedialis be considered as essentially one system and we shall usually employ the term central commissural system for them. Nn. interparataenialis and intermediodorsalis for the present are counted in the medial group, although it is somewhat doubtful whether they rightly belong there.

It is not our aim to present here the nuclear configuration of the rabbit's thalamus. There is little doubt that some delimitations and groupings of the dorsal thalamic nuclei, as suggested by cell and fiber structure and by comparative and ontogenetic observations, will have to be reconsidered in order to correlate them with the experimental results. This is to be expected because the comparative anatomical identification of some nuclei (*e.g.*, our identification of pars suprageniculata of the posterior nucleus of the rabbit) is not as certain as could be desired, and because morphological and ontogenetic observations often leave considerable freedom of interpretation. For our

present purpose, however, exact delimitations of the nuclei of the dorsal thalamus are, for the most part, inconsequential. The configuration of the thalamic nuclei, therefore, will be considered only in so far as it is relevant to the findings.

*Description of ablations in RW 10, RW 19 and RW 18.* Complete unilateral ablation of the telencephalon was undertaken in three animals (RW 10, RW 19 and RW 18). The goal was to remove the whole cerebral cortex with all olfactory structures, as well as the striatum and amygdala, without causing any other injuries. Since the telencephalon has a broad connection with the hypothalamus, which we wished to leave intact, the ideal operation should destroy the septum at the telencephalic-hypothalamic border leaving unharmed the diagonal area and it should remove the striatum and amygdala while preserving the globus pallidus and the rest of the hypothalamus. The three operations were not equally successful. The desired result was almost achieved in RW 10. Diagrams (Figs. 1 and 2) of horizontal sections of this brain show that, of the whole telencephalon, there remained on the operated side only a few cells of taenia tecta (tt.), a fragment of the septal area[1] (s.p.) and a badly damaged part of the most ventral tip of the pyriform lobe, containing small portions of the amygdala (Am.), of the periamygdaloid (Pam.) and entorhinal (En.) regions and of Ammon's formation (FA.).[2] All other parts of cortex, striatum and amygdala were removed. On the other hand a con-

[1] The septal area in the rabbit includes n. medalis septi, n. lateralis septi, n. septalis fimbrialis, n. septalis triangularis and certain other structures recognized as septal nuclei by Young (1936). Our delimitations of these nuclei in the rabbit probably correspond exactly to the delimitations of Fox (1940) in the cat but they are not always in agreement with those of Young. We do not consider the following as septal structures: 1. The anterior continuation of the hippocampus; 2. the so-called n. accumbens septi; 3. area diagonalis; 4. n. interstitialis striae terminalis. The anterior continuation of the hippocampus, the induseum griseum and, probably, certain sectors of n. septo-hippocampalis of Young are designated taenia tecta in this paper and considered to be cortex. N. accumbens septi is considered a part of the striatum. N. interstitialis striae terminalis of Young and Fox, which is probably identical with the prethalamic complex of our delimitation, and area diagonalis are held to be parts of the hypothalamus.

[2] When fragments of structures remain, it is usually difficult to decide to what extent connections with the thalamus have been preserved. In order to make our statements as cautious as possible, we shall assume the existence of normal connections whenever any fragment has not been entirely isolated.

siderable portion of the diagonal area (Diag.) and a part of the globus pallidus (P.) were ablated. The operation on RW 19 was in some respects less, in others more, satisfactory. Horizontal sections (Figs. 3 and 4) of this brain show that there remained of the telencephalon a small fragment of septum (s.p.) and a larger portion of the pyriform lobe; the latter consists of parts of the amygdaloid nuclei (Am.), some of the periamygdaloid region (Pam.), small fragments of the entorhinal (En.) and presubicular (Presub.) regions and of Ammon's formation (FA.). The operation involved also to some extent the area diagonalis (Diag.), but a considerable portion of the globus pallidus (P.), as well as the rest of the hypothalamus, remained uninjured. Moreover, at the border of the globus pallidus a narrow rim of cells of the striatum was left. In the third animal (RW 18) there remained of the telencephalon on the operated side a bit of the septum, traces of taenia tecta, a fragment of the amygdala and of the pyriform lobe with a rather large amount of the periamygdaloid region and small portions of the entorhinal and presubicular regions and of Ammon's formation. The remaining parts of the telencephalon were larger than in the other two experiments. The striatum was practically completely removed but the globus pallidus also was largely destroyed and the area diagonalis was partly involved. The rest of the hypothalamus was intact.

In no case was there any injury to the midbrain, nor was there any evidence of direct trauma to the thalamus at operation. The thalamus of RW 10 showed a slight injury produced during removal of the brain postmortem (see sections 224 and 264, Fig. 1). In RW 18, moreover, a larger damage to the anterodorsal part of the thalamus of the operated side resulted from the necessity of removing a small adherent piece of bone while the brain was being sectioned serially. At the border between thalamus and mesencephalon in RW 10 there was for some distance a minute focus of infiltration which in no way obscured the findings; it was the only lesion of this sort seen in the brains studied.

*Description of findings in RW 10, RW 19 and RW 18.* The changes in the thalamus were essentially identical in all three animals. We will begin by presenting the findings in RW 19, an animal sacrificed 28 days after operation. A horizontal series was chosen because the sharp demarcation between intact and degenerated thalamic nuclei can be appreciated best with this plane of section.

1. The epithalamus: Figs. 10–21 show the thalamus of this animal

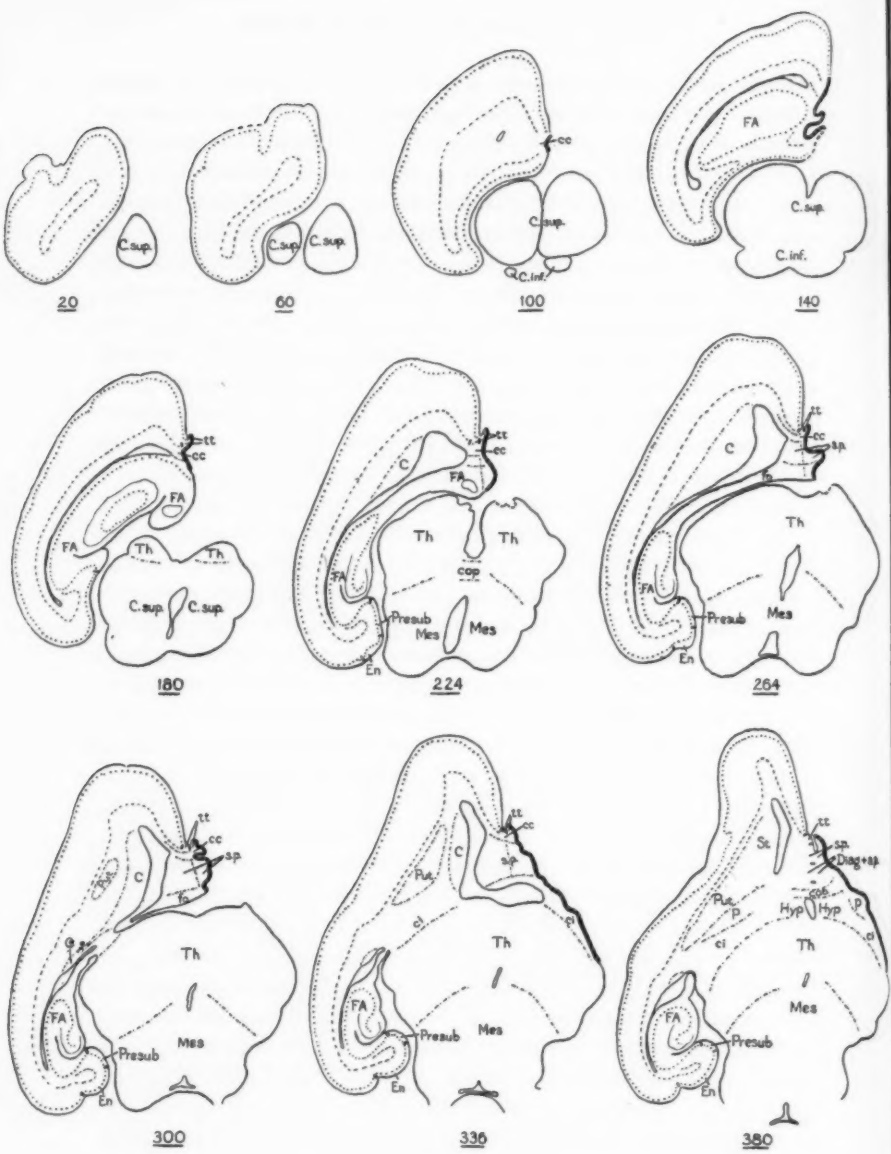
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FIG. 1

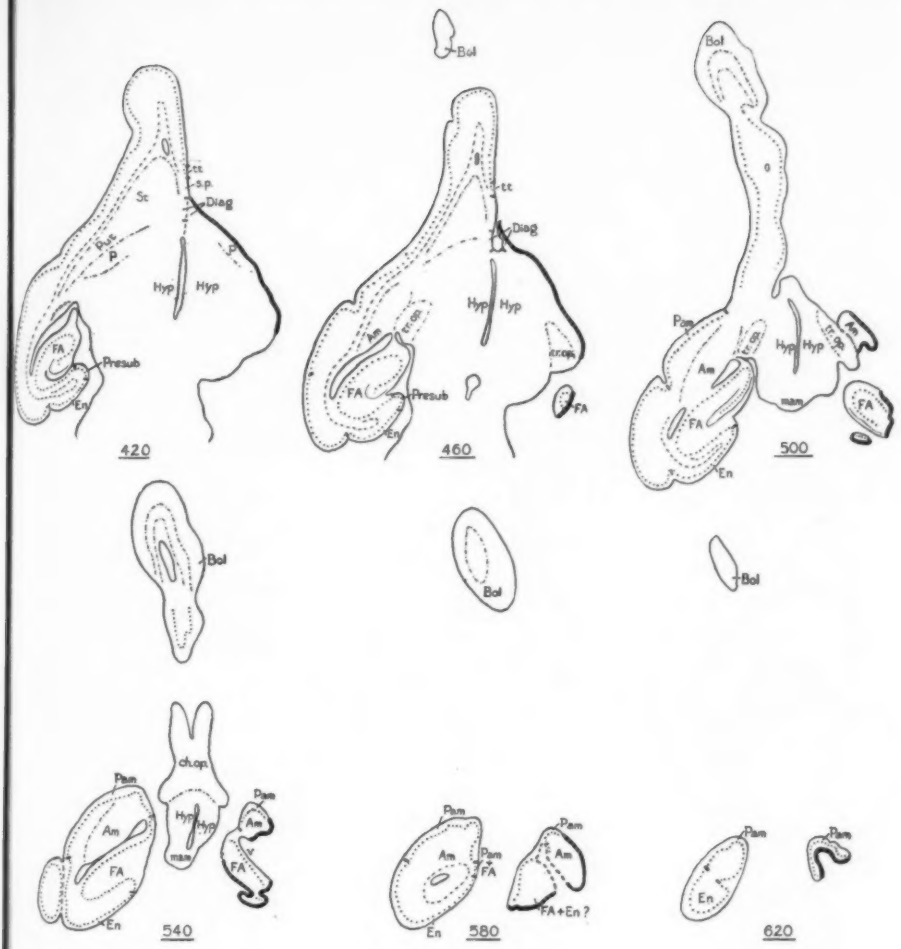


FIG. 2

FIGS. 1 AND 2. These are drawings (×2.5) made with a projector from horizontal sections of rabbit RW 10 to show the extent of the unilateral ablation of the telencephalon. The number under each drawing is the serial number of the section from which it was made. Section 20 is most dorsal, 620 most ventral. The heavy lines mark the border of the ablation. The dotted lines represent the inner limit of the first cortical layer; the dashes show the total depth of the cortex. Dots and dashes mark limits of various structures. The thin line in the region of Ammon's formation indicates fascia dentata. Broken outline (in sections 224 and 264) indicates technical imperfection of the section. Telencephalic structures not entirely destroyed on the operated side are delimited on the normal side.

Am., n. amygdalae; Bol., bulbus olfactorius; C., n. caudatus; cc., corpus callosum; ch. op., chiasma opticum; ci., capsula interna; C. inf., colliculus inferior; coa., commissura anterior; cop., commissura posterior; C. sup., colliculus superior; Diag., area diagonalis; En., regio entorhinalis; FA., formatio Ammonis; fo., fornix; Hyp., hypothalamus; mam., corpus mamillare; Mes., mesencephalon; P., globus pallidus; Pam., regio periamygdalaris; Presub., regio praesubicularis; Put., putamen; s.p., septum; St., striatum (n. caudatus and putamen); Th., thalamus; tr. op., tractus opticus; tt., taenia tecta; v., ventricle.

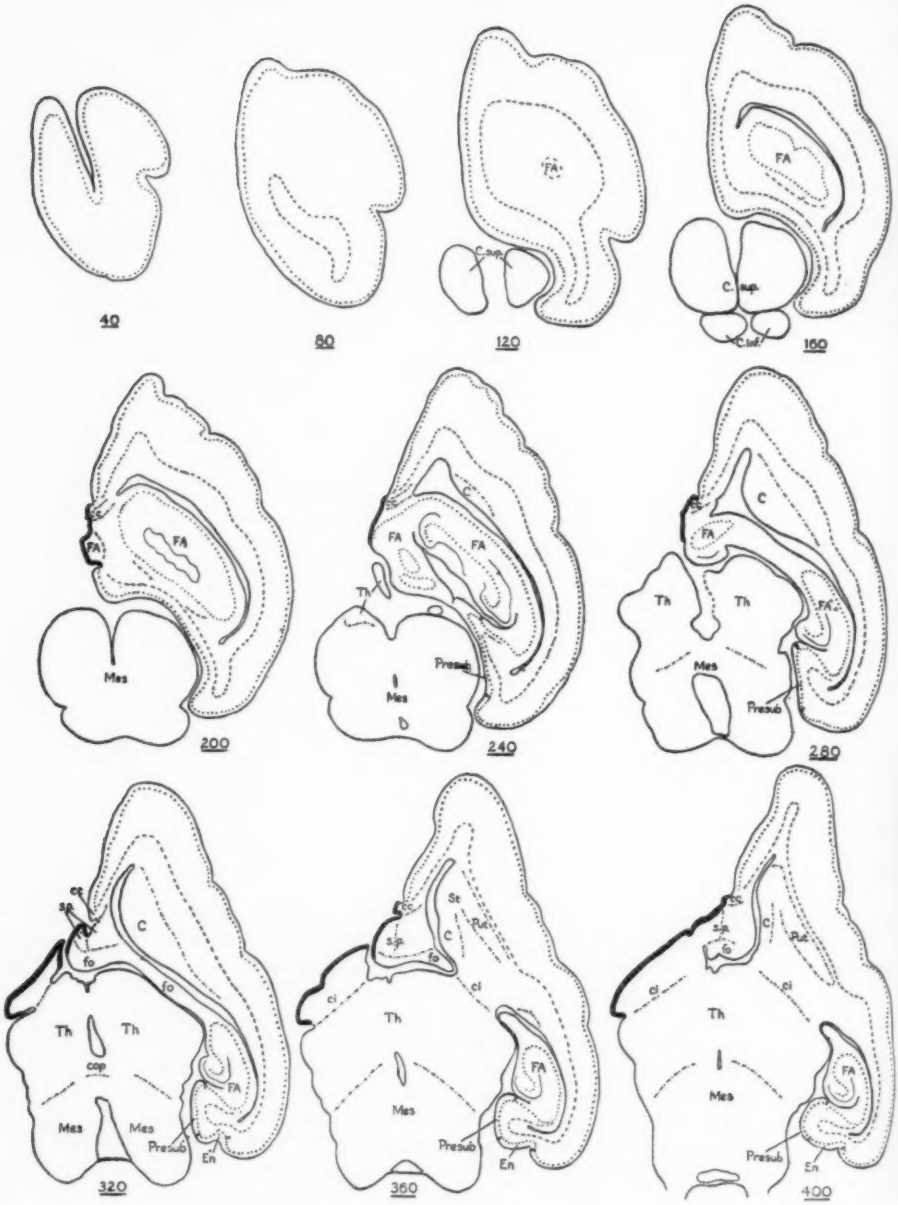
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FIG. 3

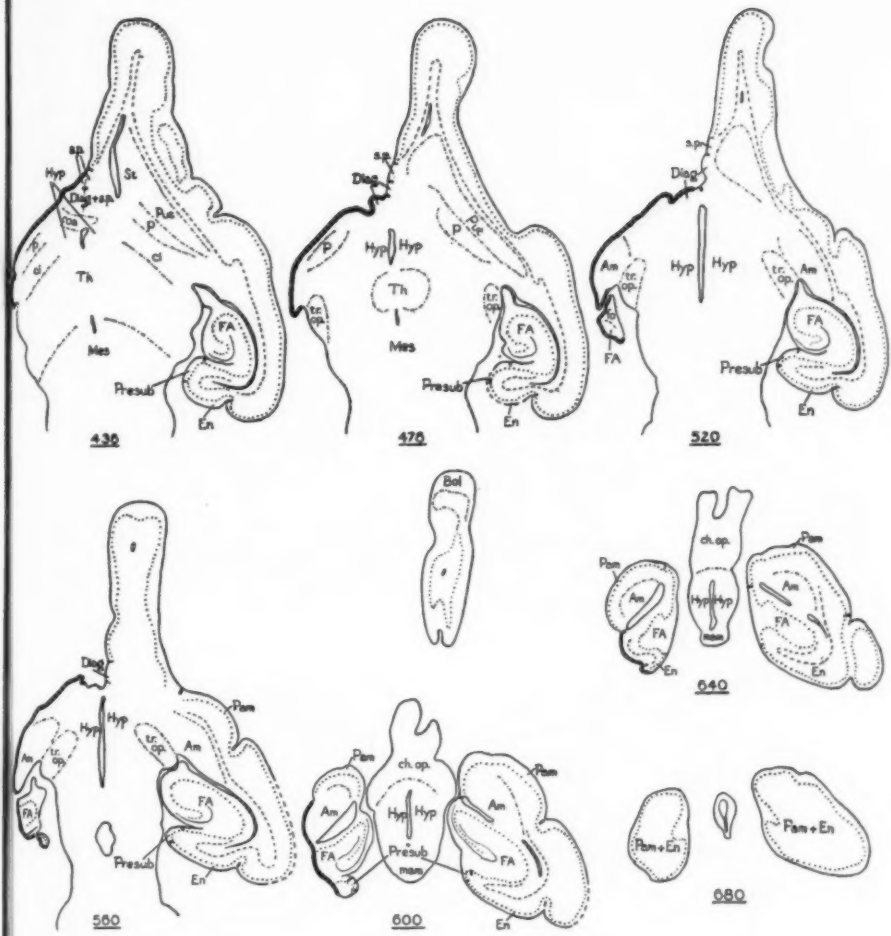



FIG. 4

FIGS. 3 AND 4. Outline drawings (×2.5) of horizontal sections of rabbit RW 19, showing the extent of the unilateral ablation of the telencephalon. The number under each drawing is the serial number of the corresponding section. Section 40 is most dorsal, 680 most ventral. In diagrams 640 and 680 the olfactory bulb was not drawn. All telencephalic structures not entirely removed on the operated side are delimited on the normal side. All markings and labels have the same meanings as in Figs. 1 and 2.

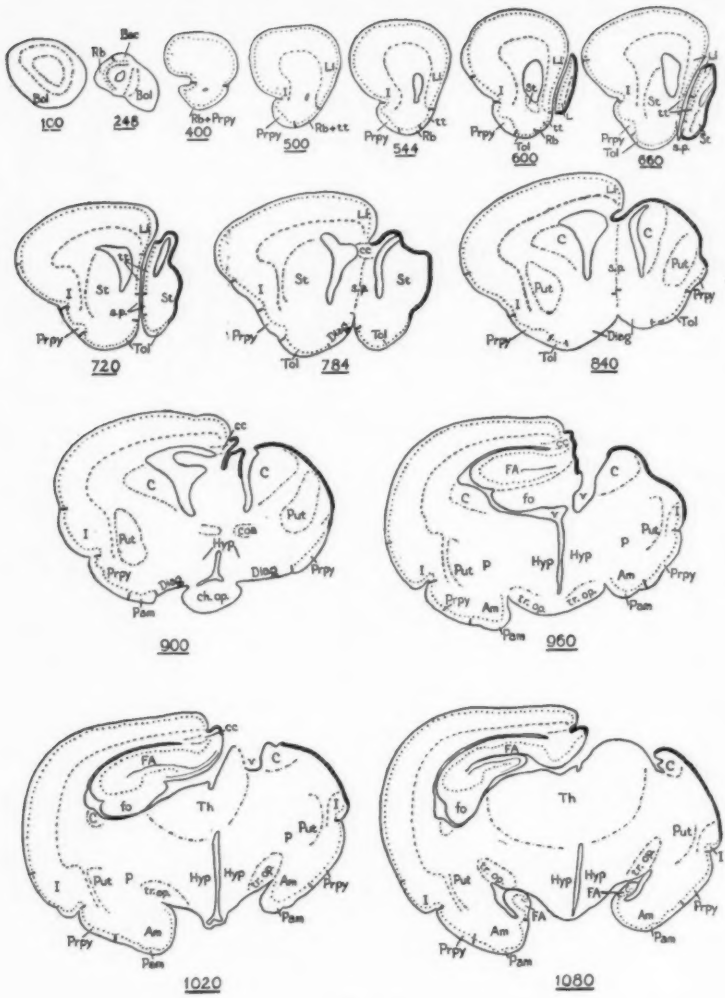



FIG. 5

FIGS. 5 AND 6. Outline drawings (×2.5) of frontal sections of rabbit RW 6, showing the extent of a unilateral operation in which our intention was to spare subcortical telencephalic structures. The number under each drawing is the serial number of the section from which the drawing was made. Drawing 100 is most oral, 1440 is most caudal. Markings have the same significance as in Figs. 1 and 2. Cortical structures not destroyed on the operated side are delimited on the normal side. A small lesion of the right cortex (left side in figures) is not shown.

Am., n. amygdalae; Bac., bulbus olfactorius accessorius; Bol., bulbus olfactorius; C., n. caudatus; cc., corpus callosum; ci., capsula interna; ch. op., chiasma

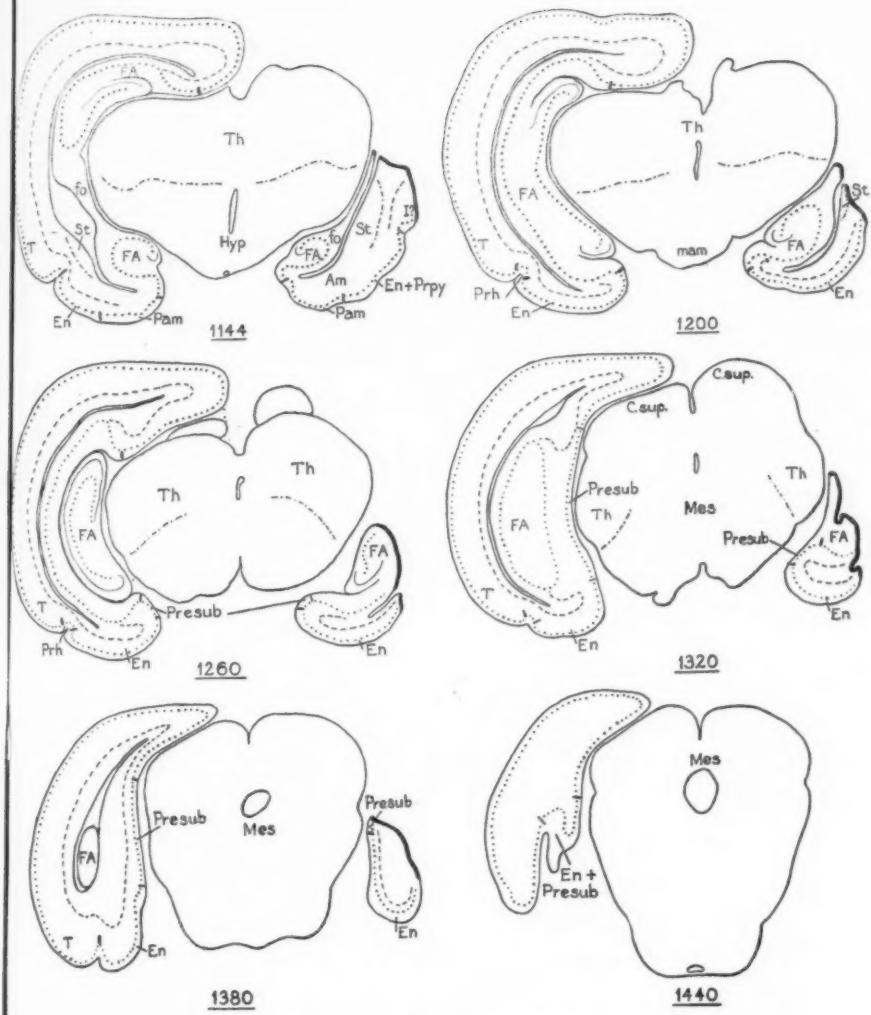



FIG. 6

opticum; coa., commissura anterior; C. sup., colliculus superior; Diag., area diagonalis; En., regio entorhinalis; FA., formatio Ammonis; fo., fornix; Hyp., hypothalamus; I., regio insularis; Li., regio limbica (infraradiata); mam., corpus mamillare, Mes., mesencephalon; Oc., regio occipitalis (area occipitalis, striata et peristriata); P., globus pallidus; Pam., regio periamygdalaris; Presub., regio praesubicularis; Prh., regio perirhinalis; Prpy., regio praepyriformis; Put., putamen Rb., regio retrobulbaris; Rs., regio retrosplenialis; s.p., septum; St., striatum; T., regio temporalis (area temporalis prima, secunda et tertia); tt., taenia tecta; Th., thalamus; Tol., tuberculum olfactorium; tr. op., tractus opticus.

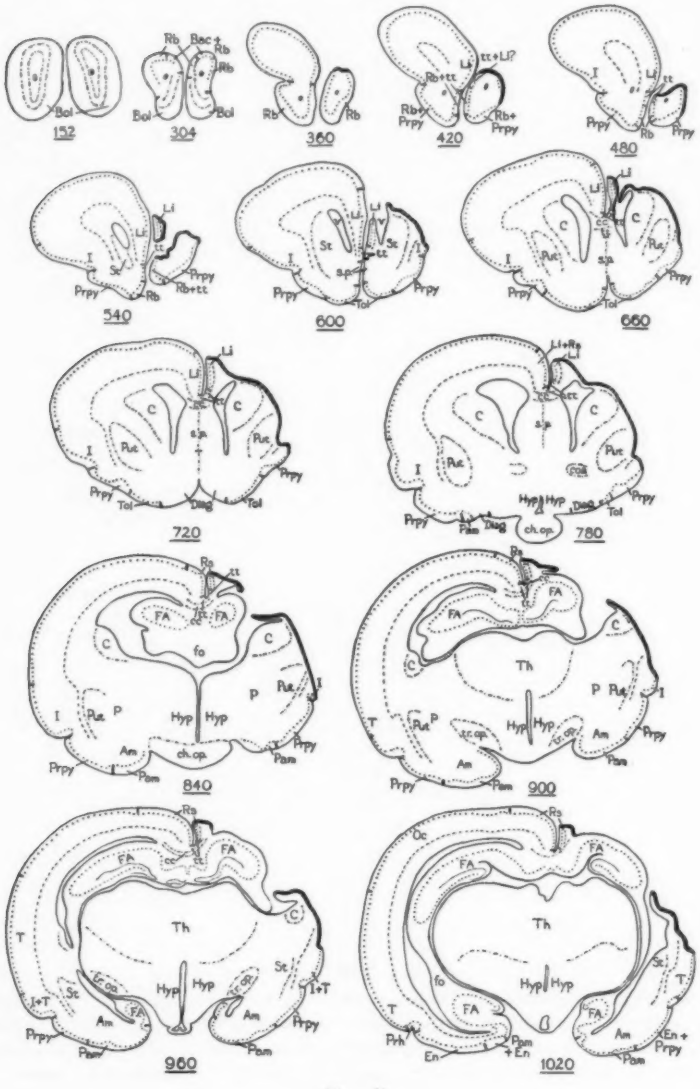



FIG. 7

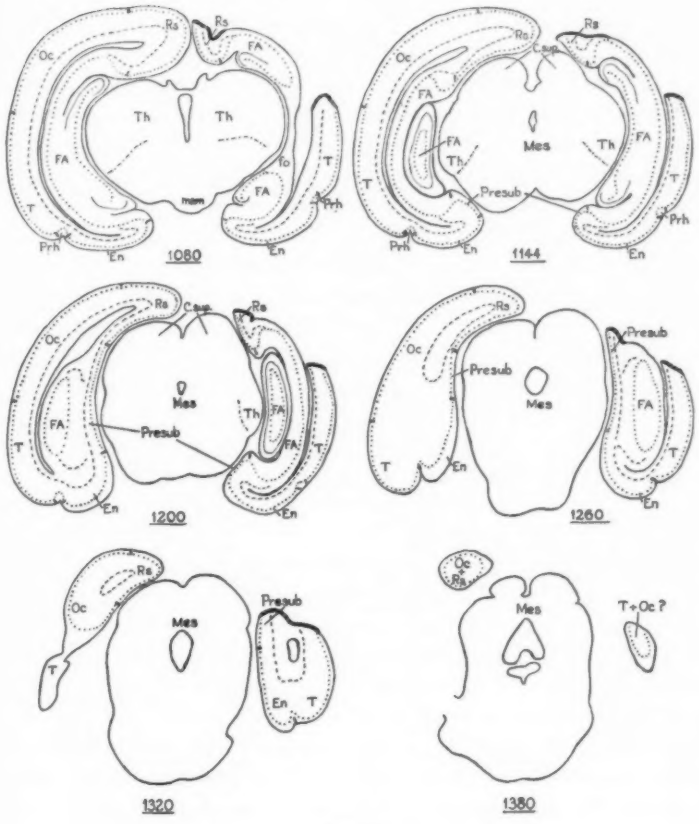



FIG. 8

FIGS. 7 AND 8. Drawings of frontal sections (×2.5) of rabbit RW 8, showing the extent of a unilateral operation in which our purpose was to spare subcortical telencephalic centers. The number under each drawing is the serial number of the corresponding section. Drawing 152 is most frontal, 1380 most caudal. A small lesion in the right cortex (left side in the drawings) is not indicated. Cortical structures not destroyed on the operated side are delimited on the normal side. Markings and labels as in Figs. 5 and 6.

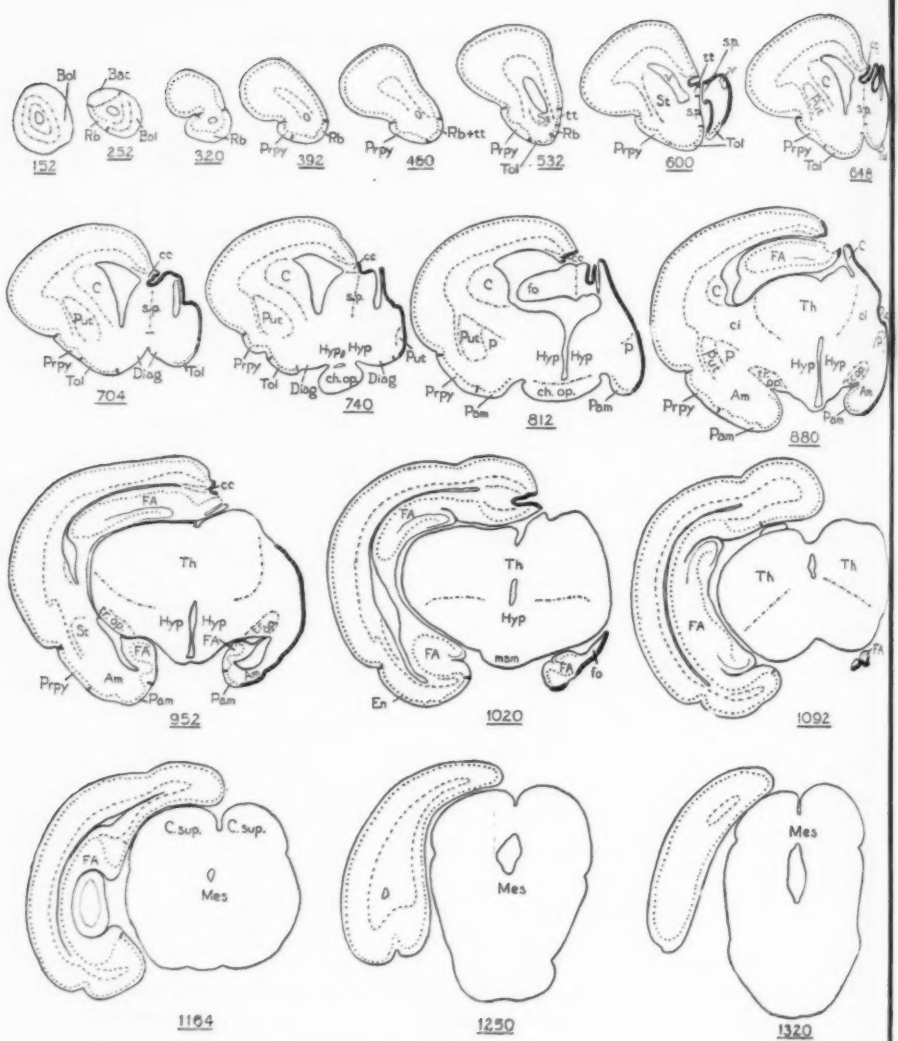
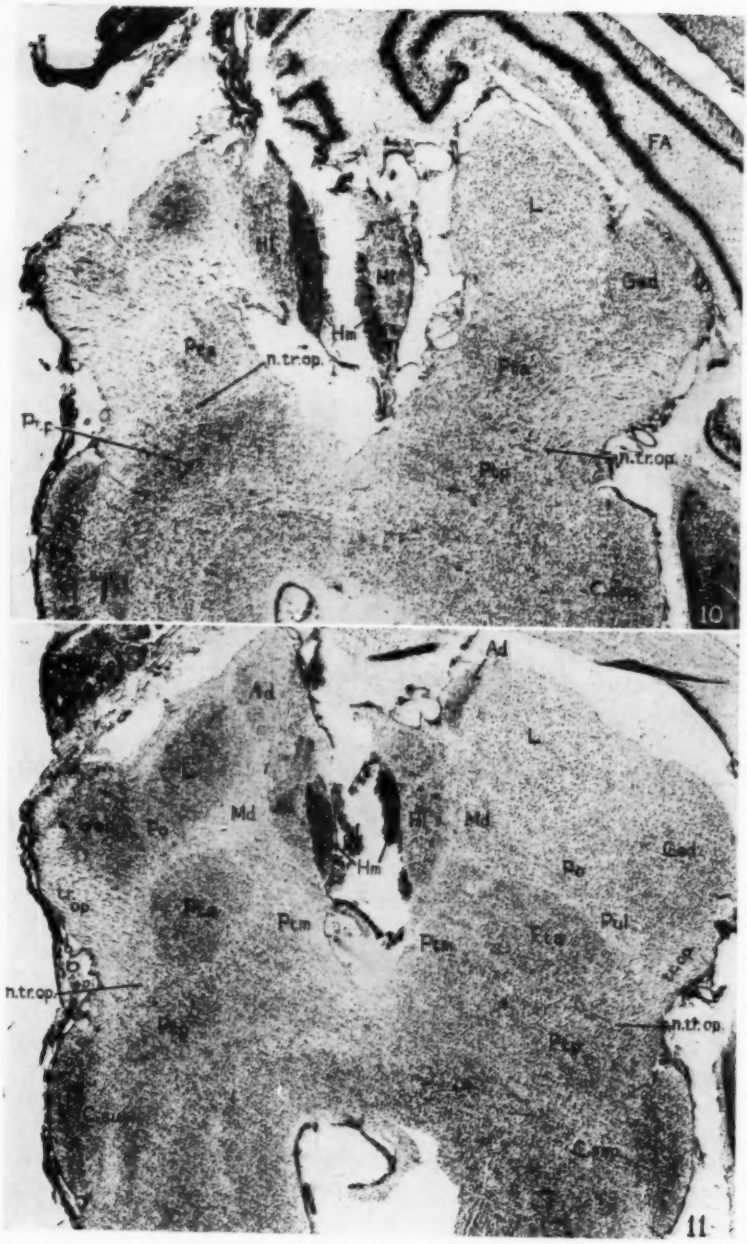



FIG. 9

FIG. 9. Drawings of frontal sections (×2.5) of rabbit RW 12, showing the extent of a unilateral subtotal ablation of the telencephalon. The number under each drawing is the serial number of the corresponding section. 152 is most frontal, 1320 most caudal. The small lesion of the right cortex (left in the drawings) is not shown. Structures not destroyed on the operated side are delimited on the normal side. All markings and labels as in Figs. 5 and 6.

on both the operated and the unoperated sides. The two sides have been cut slightly asymmetrically. Figs. 10–12 make clear that the habenular complex is quite intact. The same is true for the whole pretectal group of the epithalamus. In the pretectal group we distinguish five main elements: n. praetectalis anterior (Pta.), n. praetectalis posterior (Ptp.), the medial pretectal area (Ptm.), n. tracti optici (n. tr. op.) and n. suprageniculatus praetectalis (Sgp.). The anterior pretectal nucleus, with its characteristic shape of a biconvex lens, makes orientation of the whole configuration easy. Figs. 10–17 show, even under low magnification, that all the pretectal elements have remained intact and that the degeneration in the dorsal thalamus stops sharply at the anterior margin of these elements wherever they border the dorsal thalamic nuclei. This sharp borderline is seen for the anterior pretectal nucleus (Pta.) in Figs. 10–17, for the medial pretectal area (Ptm.) in Figs. 10–13 and for n. tracti optici (n. tr. op.) and n. suprageniculatus praetectalis (Sgp.) in Figs. 10–15. It will be noted by comparison with the normal side that the line at which degeneration stops corresponds quite exactly to the anterior limits of the pretectal elements.

The pretectal group and, particularly, the anterior pretectal element appear, however, to be much richer in glia on the operated side than on the normal. Since the corticotectal fibers run through this region it seems probable that this fact accounts for the increase in glia in the pretectal group. At any rate, one can convince oneself easily that the increase of glia cells is not associated with any degeneration of the nerve cells and that the latter remain unchanged. Fig. 22 shows, under higher power, the anterior pretectal nucleus and its surroundings. The normal architectonics of n. praetectalis anterior, n. praetectalis posterior and the medial pretectal area contrasts with the completely degenerated pulvinar, n. mediodorsalis and n. posterior. In the upper right corner of the figure the medial pretectal area adjoins the intact habenular nuclei, which in this section are about to disappear. At the lower left margin the completely preserved n. tracti optici is seen in part. Fig. 23, at the same magnification (× 30), shows n. suprageniculatus praetectalis entirely intact. The few unchanged cells immediately in front of it probably still belong to n. tracti optici. N. praetectalis anterior is, of course, also quite unchanged, whereas




FIGS. 10–11

the adjoining nuclei of the dorsal thalamus are everywhere most severely degenerated.

The last group of the epithalamus is the paraventricular complex. For the most part this is an elongated ribbon of cells lying just beneath the ependyma. It begins at the oroventral pole of the thalamus where it merges with the periventricular gray of the hypothalamus. It then ascends along the ventricular wall dorsally and turns backward sharply in a semicircular fashion until it reaches the habenula. It lies ventral to the latter and merges ventrocaudally with the periventricular gray of the midbrain. In cell preparations its caudal portion seems also to fuse with the medial pretectal area. We designate the longer, larger celled sector of this complex as n. paraventricularis anterior and the caudal extension as n. paraventricularis posterior (Para. and Parp. in Figs. 12–17). The paraventricular complexes of the two sides fuse in the midline and the fused portion merges ventrally with the midline structures of the dorsal thalamus. Since the paraventricular complex thus cannot be demarcated clearly from the midline structures of the dorsal thalamus, it is not easy to prove that the whole complex really remains intact. If, however, for the time being, the part which fuses with the dorsal thalamus is omitted and only the main portion which lies along the ependyma is considered, then it is clear, as Figs. 12–15

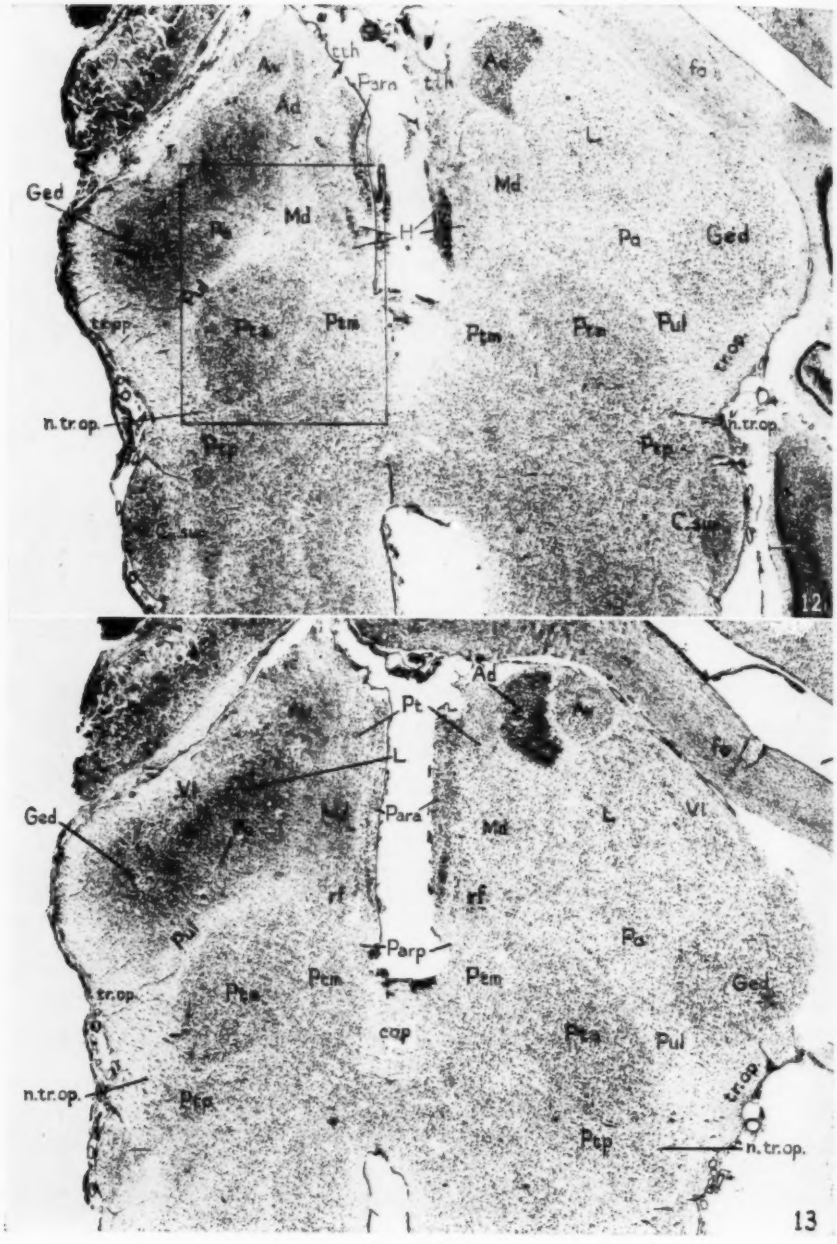
FIG. 10. RW 19, SECTION 268, × 10.

FIG. 11. RW 19, SECTION 284, × 10.

FIGS. 10–21 are low power photomicrographs of horizontal sections of RW 19. Fig. 10 is most dorsal, Fig. 21 most ventral. See Figs. 3 and 4 for location of sections and extent of the operation.

The cell pattern in the right half of Figs. 10–21 is entirely normal. Note that the habenular nuclei (Hm. and Hl., torn during technical preparation) and the pretectal elements (n. praetectalis anterior, Pta.; n. praetectalis posterior, Ptp.; area praetectalis medialis, Ptm.; and n. tracti optici, n. tr. op.) are quite intact on the operated side (left) although the latter show increased gliosis. Observe that the degeneration stops sharply at the borders of these groups. Note that the glial reaction in the degenerated elements of the dorsal thalamus varies.

Ad., n. anterodorsalis; C. sup., colliculus superior; FA., formatio Ammonis; Ged., corpus geniculatum laterale dorsale; Hl., n. habenularis lateralis; Hm., n. habenularis medialis; L., n. lateralis; Md., n. mediodorsalis; n. tr. op., n. tracti optici; Po., n. posterior; Pta., n. praetectalis anterior; Ptm., area praetectalis medialis; Ptp., n. praetectalis posterior; Pul., pulvinar; tr. op., tractus opticus.


Ged
Md
Pa
Ptm
Ptp
Pul
n.tr.op.
tr.op
Ad
Aw
Para
Parp
Pt
L
Vl
rf
cap
fo
12
13

FIGS. 12–13

plainly show, that this part of the complex at least did not degenerate. We shall return to the more exact demarcation of the paraventricular complex below. Here we shall anticipate our conclusion that the whole paraventricular complex remains quite intact after removal of the telencephalon.

2. The dorsal thalamus: A glance at Figs. 10–21 reveals that, in contrast with the epithalamic nuclei, all dorsal thalamic nuclei are profoundly affected. Completely degenerated are the anterior group (n. anterodorsalis, Ad., n. anteroventralis, Av., and n. anteromedialis, Am., Figs. 11–17), the medial group (n. mediodorsalis, Md., and n. medioventralis, Mv., Figs. 11–21), the dorsolateral group (n. lateralis, L., n. posterior, Po., and the pulvinar, Pul., Figs. 10–19), the ventral group (n. ventroanterior, Va., all elements of the ventrobasal complex, Vb., Var., Vme., the ventrolateral complex, Vl, and the angular nucleus, Ang., Figs. 13–21), the dorsal lateral geniculate body (Ged., Figs. 10–17) and both divisions of the medial geniculate body (Gid. and Giv., Figs. 15–20). It is probably literally true that not a single nerve cell in these elements has remained intact. Most of the cells have disappeared completely; the rest are disintegrating or are so severely changed that one can speak of complete degeneration of all these elements.

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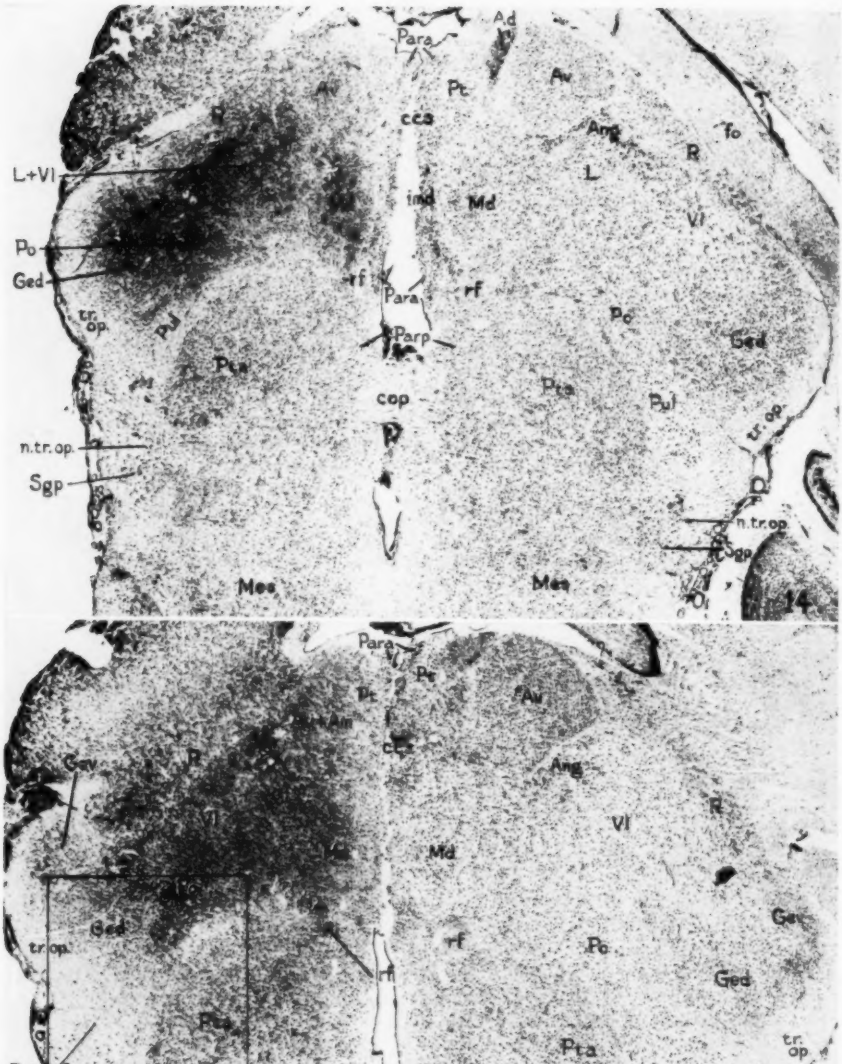
FIG. 12. RW 19, SECTION 296, × 10.

FIG. 13. RW 19, SECTION 312, × 10.

Note that the habenular complex, all pretectal elements and the paraventricular complex (Para. and Parp.) are unaffected on the left, whereas all dorsal thalamic elements are entirely degenerated on this side. N. paraventricularis anterior is not cut symmetrically. It appears on the operated side in Fig. 12, on both sides in Fig. 13. Compare the pattern of the normal dorsal thalamic nuclei on the right with the glial reaction pattern on the operated side.

The area outlined in Fig. 12 is shown under higher power in Fig. 22.

Ad., n. anterodorsalis; Av., n. anteroventralis; cop., commissura posterior; C. sup., colliculus superior; fo., fornix; Ged., corpus geniculatum laterale dorsale; H., habenular complex; L., n. lateralis; Md., n. mediodorsalis; n. tr. op., n. tracti optici; Para., n. paraventricularis anterior; Parp., n. paraventricularis posterior; Po., n. posterior; Pt., n. parataenialis; Pta., n. praetectalis anterior; Ptm., area praetectalis medialis; Ptp., n. praetectalis posterior; Pul., pulvinar; rf., fasciculus retroflexus Meynerti; tr. op., tractus opticus; tth., taenia thalami; Vl., ventrolateral complex.


Para
Ad
Pt
Av
cca
Ang
fo
R
L
L+VI
ind
Md
VI
Po
Ged
rf
Para
rf
tr. op.
Pul
Parp
Po
Ged
Pta
cop
Pta
Pul
tr. op.
n.tr.op.
Sgp
n.tr.op
Sgp
Mes
Mes
14
Para
Pc
Pt
Av
Ang
Ged
R
VI
R
Md
Ged
rf
Po
Ged
tr. op.
rf
Pta
tr. op.
Pul+
Gid
Sgp
Mes
Mes
Sgp
Pul+
Gid
15

FIGS. 14–15

Since there is rather general agreement that all the nuclear groups just mentioned do degenerate after ablation of the cortex, a detailed description of the findings seems superfluous. It will be noted, however, that with complete ablation of the telencephalon all these nuclei are degenerated in their whole extent, and that there are no subdivisions or sectors of them which remain better preserved than others. Further, *it should be emphasized that the postmedial group* (n. parafascicularis, Pf., and centrum medianum, Cm., Figs. 16 and 17) *has also completely degenerated. Finally, a finding of special importance is the fact that all midline structures of the dorsal thalamus have degenerated as severely as have all other dorsal thalamic elements.* A closer examination of Fig. 14 reveals that n. intermediodorsalis (imd.) is obviously severely affected on the operated side. Since, unfortunately, the preparation is torn in the middle, this picture is not entirely convincing. In Figs. 15 to 21, however, it may be seen clearly that for all practical purposes the degeneration of the dorsal thalamic nuclei stops

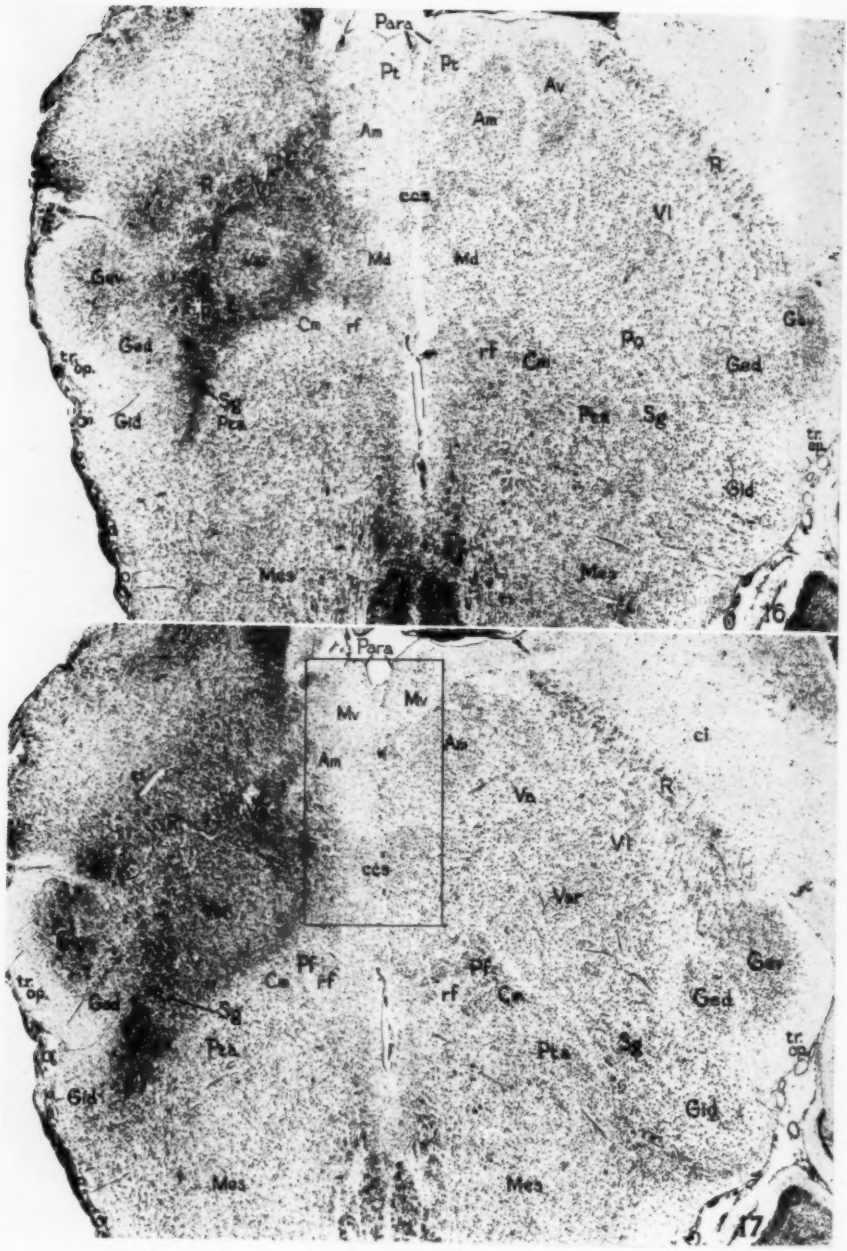
FIG. 14. RW 19, SECTION 328, × 10.

FIG. 15. RW 19, SECTION 360, × 10.

In the pretectal configuration n. suprageniculatus praetectalis (Sgp.) has been cut through. Note that this element, all other pretectal nuclei and the paraventricular complex remain unchanged on the operated side. Observe the demarcation of n. suprageniculatus from the dorsal division of the medial geniculate (Gid.) on the normal side (Fig. 15) and note that the latter and the pulvinar (Pul.) have disappeared on the operated side. N. paraventricularis anterior (Para.) has been cut twice in Fig. 14 and in its oroventral extremity in Fig. 15. Note the beginning of the midline nuclei (imd. and ccs.). Observe that all dorsal thalamic elements, including the midline nuclei, have degenerated in their whole extent on the operated side. Note the degeneration in the reticular complex (R.) and the intactness of the ventral lateral geniculate body (Gev.).

The area outlined in Fig. 15 is shown at higher magnification in Fig. 23.

Ad., n. anterodorsalis; Am., n. anteromedialis; Ang., n. angularis; Av., n. anteroventralis; ccs., central commissural system; cop., commissura posterior; fo., fornix; Ged., corpus geniculatum laterale dorsale; Gev., corpus geniculatum laterale ventrale; Gid., corpus geniculatum mediale, pars dorsalis; Giv., corpus geniculatum mediale, pars ventralis; imd., n. intermediodorsalis; L., n. lateralis; Md., n. mediodorsalis; Mes., mesencephalon; n. tr. op., n. tracti optici; Para., n. paraventricularis anterior; Parp., n. paraventricularis posterior; Po., n. posterior; Pt., n. parataenialis; Pta., n. praetectalis anterior; Pul., pulvinar; R., reticular complex; rf., fasciculus retroflexus Meynerti; Spg., n. suprageniculatus praetectalis; tr. op., tractus opticus; Vl., ventrolateral complex.


Para
Pt
Pc
Av
Am
Am
R
ccs
VI
Md
Md
Gev
Cm
rf
rf
Cm
Po
Ged
tr. op.
Sg
Pta
Pta
Sg
Gld
Mes
Mes
16
Para
Mv
Mv
Am
Am
ci
R
Vm
VI
ccs
Var
Gev
Pf
Pf
Cm
rf
rf
Cm
Ged
tr. op.
Ged
Sg
Pta
Pta
Sg
tr. op.
Gld
Gld
Mes
Mes
17

FIGS. 16–17

sharply at the midline and that consequently all midline unpaired structures must have degenerated on the operated side. There is, of course, also no question that all the so-called intralaminar nuclei (which we designate, together with some midline structures, as the central commissural system, ccs.) have completely disappeared.

Fig. 24 shows the midline and its surroundings under higher power. For comparison a corresponding section from a normal rabbit is shown in Fig. 25. From Fig. 24 it will be noted that hardly any cells persist on the operated side of the midline and that the midline structures associated with n. medioventralis and n. anteromedialis, as well as the rest of the commissural system, have disappeared on this side. Fig. 25 shows how the midline structures look at this level in the normal brain. Fig. 26 shows the midline and its surroundings further ventrally. Here too the degeneration obviously stops abruptly along the midline. However, to demonstrate conclusively that n. intermediodorsalis also degenerates completely on the operated side, a series, technically perfect in the midline, is necessary. Figs. 27–29 show the thalamus of RW 10 somewhat more magnified than the survey pictures of RW 19. The animal was sacrificed 19 days after operation and quite a few cells still persist throughout the thalamus on the affected side. We shall

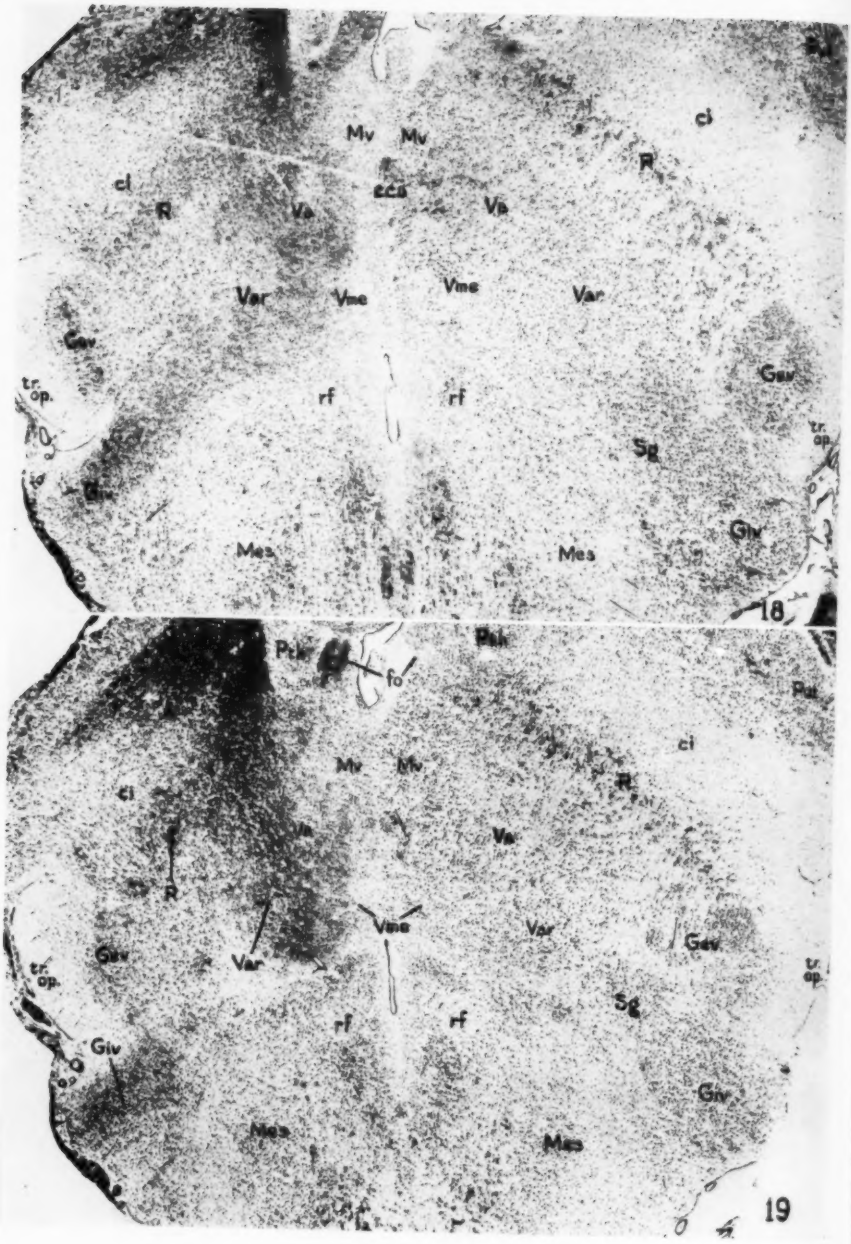
FIG. 16. RW 19, SECTION 380, × 10.

FIG. 17. RW 19, SECTION 400, × 10.

Observe again that all midline elements on the left have degenerated as severely as all other dorsal thalamic nuclei and that their degeneration stops at the midline. Note that centrum medianum (Cm.) and n. parafascicularis (Pf.) have disappeared completely on the left. Compare the pattern of glial reaction in the degenerated elements with the normal cell pattern on the right. Note that the ventral lateral geniculate body (Gev.) is not changed on the left except for some increase of glia but that the reticular complex (R.) is severely degenerated.

The area outlined in Fig. 17 is shown under higher power in Fig. 24.

Am., n. anteromedialis; Av., n. anteroventralis; ci., capsula interna; Cm., centrum medianum; ccs., central commissural system; Ged., corpus geniculatum laterale dorsale; Gev., corpus geniculatum laterale ventrale; Gid., corpus geniculatum mediale, pars dorsalis; Md., n. mediodorsalis; Mes., mesencephalon; Mv., n. medioventralis; Para., n. paraventricularis anterior; Pf., n. parafascicularis; Po., n. posterior; Pt., n. parataenialis; Pta., n. praetectalis anterior; R., reticular complex; rf., fasciculus retroflexus Meynerti; Sg., pars supragenicula ta of n. posterior; tr. op., tractus opticus; Va., n. ventroanterior; Var., pars arcuata of the ventrobasal complex; Vl., ventrolateral complex.


Mv
Mv
ci
R
ci
R
Va
ecb
Vb
Var
Vme
Vme
Var
Gsv
tr. op.
rf
rf
Sg
tr. op.
Giv
Giv
Mes
Mes
18
Pal
fo
Pal
ci
Mv
Mv
R
ci
Va
R
Vme
Var
Gsv
Gsv
tr. op.
tr. op.
Sg
rf
rf
Giv
Giv
Mes
Mes
19

FIGS. 18–19

return to this question below. It should be mentioned first that in Fig. 27 there are perhaps some cell changes in the anterior group of nuclei on the left side—the result of a small lesion in the left limbic cortex. Otherwise all the nuclei on the left are intact. Fig. 27 just touches the area of fusion of the paraventricular complex with n. intermediodorsalis. All the dorsal thalamic nuclei on the right are severely degenerated. The pretectal elements on the other hand (only a part of the anterior pretectal nucleus is visible) and the paraventricular complex are quite intact. The area of fusion of the paraventricular complex with n. intermediodorsalis (indicated by x) is somewhat doubtfully intact. In the midline it appears rather normal but more laterally a definite dropping out of cells seems to have occurred. Fig. 28 shows a section about 0.4 mm. further ventral, *i.e.*, below the fusion of the paraventricular complex with the midline structures of the dorsal thalamus. The paraventricular complex plainly is not affected but n. intermediodorsalis and the central commissural system are severely degenerated on the operated side although many cells still persist. It will be noted that the degeneration in n. intermediodorsalis starts abruptly at the right side of the midline. All other dorsal thalamic elements of course have degenerated. Fig. 29 shows a still more ventral level of the same brain. Again n. paraventricularis anterior is intact but n. intermediodorsalis and the central commissural system show severe degeneration to the right of the midline.

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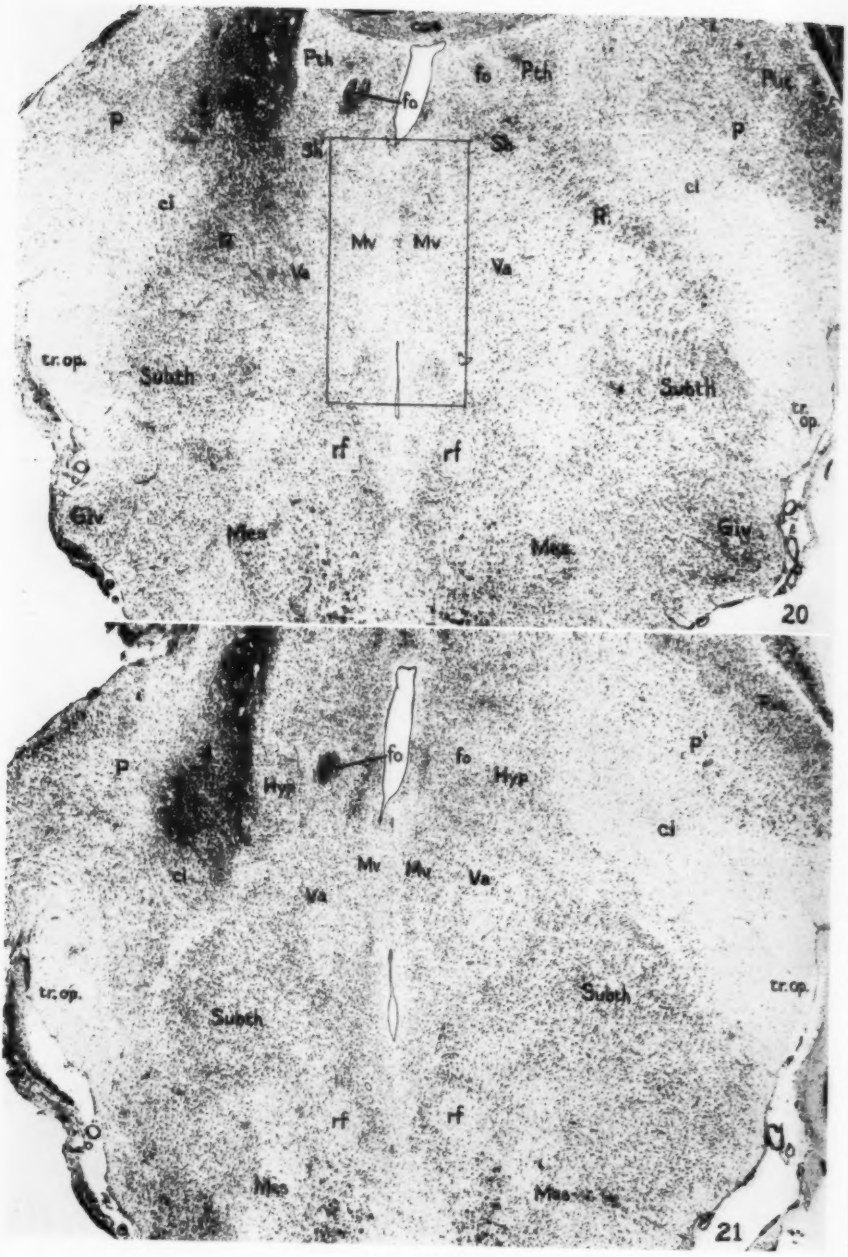
FIG. 18. RW 19, SECTION 420, × 10.

FIG. 19. RW 19, SECTION 444, × 10.

In the dorsal thalamus mainly the ventral group and the medial geniculate are seen. Observe again that all midline nuclei, together with all other dorsal thalamic elements, have degenerated in their whole extent. Note the lack of any obvious cell changes in the ventral lateral geniculate body (Gev.). In Fig. 19 the beginning of the hypothalamus (Pth.) is seen, lateral to the fornix (fo.). The latter shows intense gliosis on the left.

ccs., central commissural system; ci., capsula interna; fo., fornix; Gev., corpus geniculatum laterale ventrale; Giv., corpus geniculatum mediale, pars ventralis; Mes., mesencephalon; Mv., n. medioventralis; Pth., prethalamic complex; Put., putamen; R., reticular complex; rf., fasciculus retroflexus Meynerti; Sg., pars supragenicula ta of n. posterior; tr. op., tractus opticus; Va., n. ventroanterior; Var., pars arcuata of the ventrobasal complex; Vme., pars medialis of the ventrobasal complex.




FIGS. 20–21

However, horizontal sections are not well suited for study of the area of fusion of the paraventricular complex and the midline structures of the dorsal thalamus; the relationships can be seen better in frontal preparations. Figs. 30–32 are frontal sections showing the midline and its surroundings of rabbit RW 18. The animal was killed 28 days after operation. In Fig. 30 the oral end of the thalamus has been cut at the place where both thalami have just completed their junction in the midline. The transection is somewhat asymmetrical, cutting the normal half slightly more caudad than the operated side. On the left side n. parataenialis (Pt.) and n. medioventralis (Mv.) can be seen together with part of n. anteromedialis (Am.). On the right side n. parataenialis and n. medioventralis are severely degenerated. Some cells visible at the right margin of the picture do not belong to the thalamus. N. paraventricularis anterior is entirely intact on both sides. Their fused part also is well preserved. No midline structures of the dorsal thalamus are yet visible. Fig. 31 shows a section about 0.6 mm. more caudad. On the normal side n. parataenialis, n. anteromedialis and n. medioventralis are seen. (N. medioventralis, however, is not entirely intact in this animal). In the midline the beginning of the rhomboidal division of the central commissural system is seen; it fuses dorsally with n. interparataenialis. N. interparataenialis in turn fuses with the paraventricular complex. On the operated side n. paraventricularis anterior obviously is unchanged. At the place of fusion with n. interparataenialis some dropping out of cells seems to have occurred. But below the fusion area it is obvious that all the midline structures have degenerated on the operated side. Fig. 32

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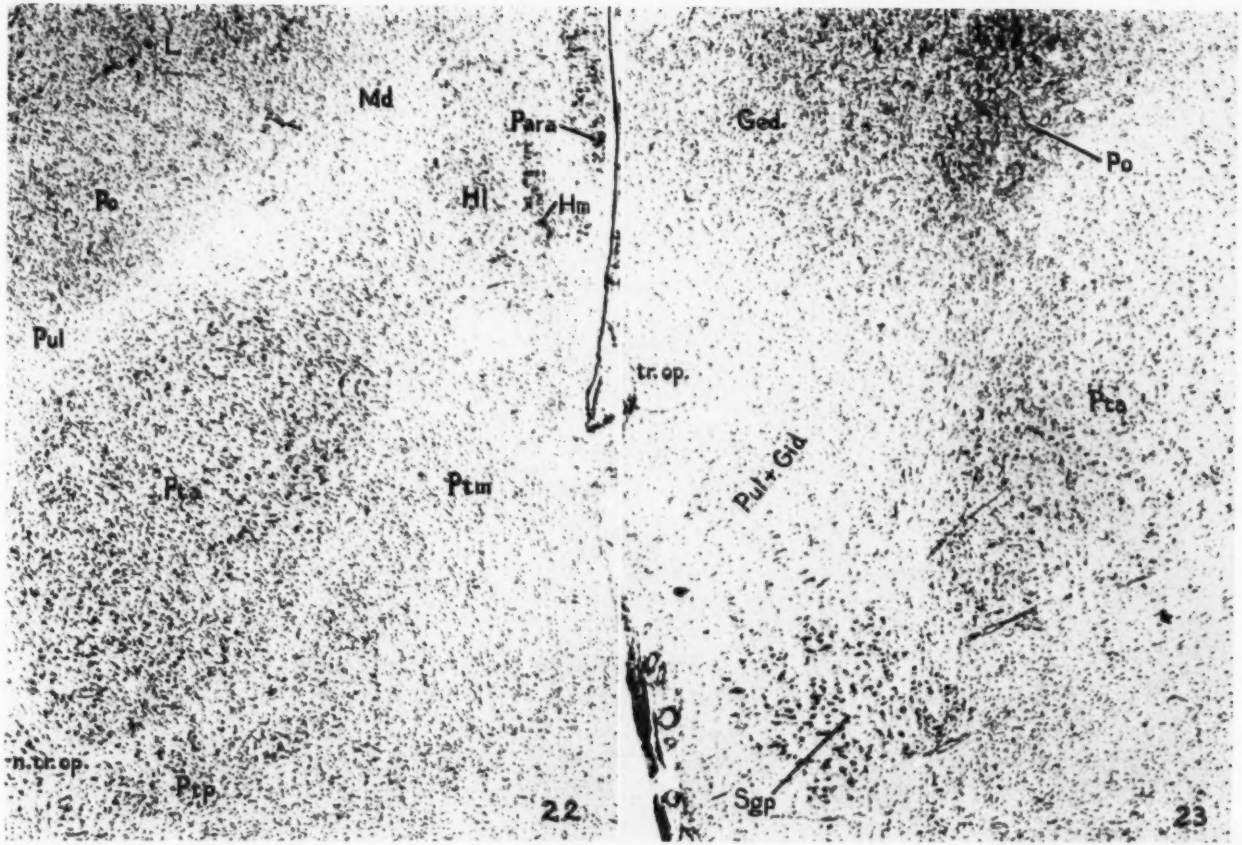
Fig. 20. RW 19, Section 460, × 10.

Fig. 21. RW 19, Section 480, × 10.

These figures show the most ventral parts of the thalamus. The ventral limit is seen in Fig. 21. N. ventroanterior (Va.) and n. medioventralis (Mv.) are degenerated in their whole extents. They may be compared with the hypothalamus (Hyp.) and subthalamus (Subth.) which show little or no alteration.

The area outlined in Fig. 20 is shown under higher power in Fig. 26.

ci., capsula interna; coa., commissura anterior; fo., fornix; Giv., corpus geniculatum mediale, pars ventralis; Hyp., hypothalamus; Mes., mesencephalon; Mv., n. medioventralis; P., globus pallidus; Put., putamen; Pth., prethalamic complex; R., reticular complex; rf., fasciculus retroflexus Meynerti; Sh., suprahypothalamic group; Subth., subthalamus; tr. op., tractus opticus; Va., n. ventroanterior.


L
Md
Para
Hl
Hm
Po
Pul
tr. op.
Pta
Ptm
n. tr. op.
Ptp
22
Ged.
Po
Pta
Pul + Gid
Sgp
23

FIGS 22-23

shows the fusion of the paraventricular complex with n. intermediodorsalis. On the normal side may be seen the habenular nuclei (Hl. and Hm.), a part of n. mediodorsalis (Md.), the narrow rim of n. paraventricularis anterior and n. intermediodorsalis (imd.) fusing dorsally with the paraventricular complex and ventrally with the central commissural system (ccs.). Still further ventrally the medial division of the ventrobasal complex (Vme.) is visible. On the operated side n. paraventricularis anterior and the habenular nuclei are intact. N. intermediodorsalis and the whole central commissural system on the right have nearly completely disappeared, together with all other dorsal thalamic elements. Since, wherever the respective structures were clearly recognizable, the paraventricular complex remained intact while n. intermediodorsalis and other dorsal thalamic elements were severely degenerated, and since in the area of fusion of these two groups the unaffected cells easily could belong to the paraventricular complex and the degenerated cells to the dorsal thalamus, we feel justified in concluding that the paraventricular complex remained unchanged in these three experiments and that all the midline structures of the dorsal thalamus degenerated. We suggest, therefore, that the paraventricular complex, which is not clearly separable anatomically from the midline structures of the dorsal thalamus, can be separated from them by experiment.

FIGS. 22-23

FIG. 22. RW 19, SECTION 296, × 30. This shows the area outlined in Fig. 12. Note the completely normal cell pattern of n. praetectalis anterior (Pta.), n. praetectalis posterior (Ptp.), area praetectalis medialis (Ptm.) and n. tracti optici (n. tr. op.). Compare these structures with the very severely degenerated pulvinar (Pul.), n. posterior (Po.), n. lateralis (L.) and n. mediodorsalis (Md.). At the upper right the ventral extremity of the unaffected habenular complex and a part of the paraventricular complex are seen.

FIG. 23. RW 19, SECTION 360, × 30. This shows the area outlined in Fig. 15. Observe the sharp border between the unchanged n. praetectalis anterior (Pta.) and n. suprageniculatus praetectalis (Sgp.) and the degenerated pulvinar (Pul.), medial geniculate (Gid.) and n. posterior (Po.).

Ged., corpus geniculatum laterale dorsale; Gid., corpus geniculatum mediale, pars dorsalis; Hl., n. habenularis lateralis; Hm., n. habenularis medialis; L., n. latralis; Md., n. mediodorsalis; n. tr. op., n. tracti optici; Para., n. paraventricularis anterior; Po., n. posterior; Pta., n. praetectalis anterior; Ptm., area praetectalis medialis; Ptp., n. praetectalis posterior; Pul., pulvinar; Sgp., n. suprageniculatus praetectalis; tr. op., tractus opticus.

FIGS. 24–26

Although all dorsal thalamic nuclei have degenerated, examination of Figs. 10–21 shows that the character of the degeneration varies greatly in different nuclear groups and at times in different portions of a single element. These differences are due to variations in the character of the glial reaction in separate elements. For a histopathological account of glial proliferation in the thalamus reference should be made to Nissl's work (1913). The fact that different nuclei, or parts of them, respond to cortical ablation with different glial reactions, thus forming a characteristic pathological pattern, is of value for checking the delimitations and subdivisions of the thalamic elements as suggested by cell and fiber structure. Broadly speaking one may divide the degenerated nuclei into those showing slight glial proliferation and those showing intense reaction, with intermediate forms between them. The differences in glial reaction, at least after 28 days, are not purely quantitative, but we shall not discuss this question now. The nuclei which react with only a slight gliosis are the nuclei of the midline, n. parataenialis, n. anteromedialis, n. medioventralis and n. mediodorsalis in certain sectors (Figs. 11–21). This type of reaction is also seen in the dorsal division of the medial geniculate body (Gid.) in sharp contrast with the ventral division of this body (Giv.) (Figs. 15–20). The reaction in the pulvinar complex is interesting. In Figs. 11–14 the complex is not subdivided on the normal side because under

FIGS. 24–26

FIG. 24. RW 19, SECTION 400, × 30.

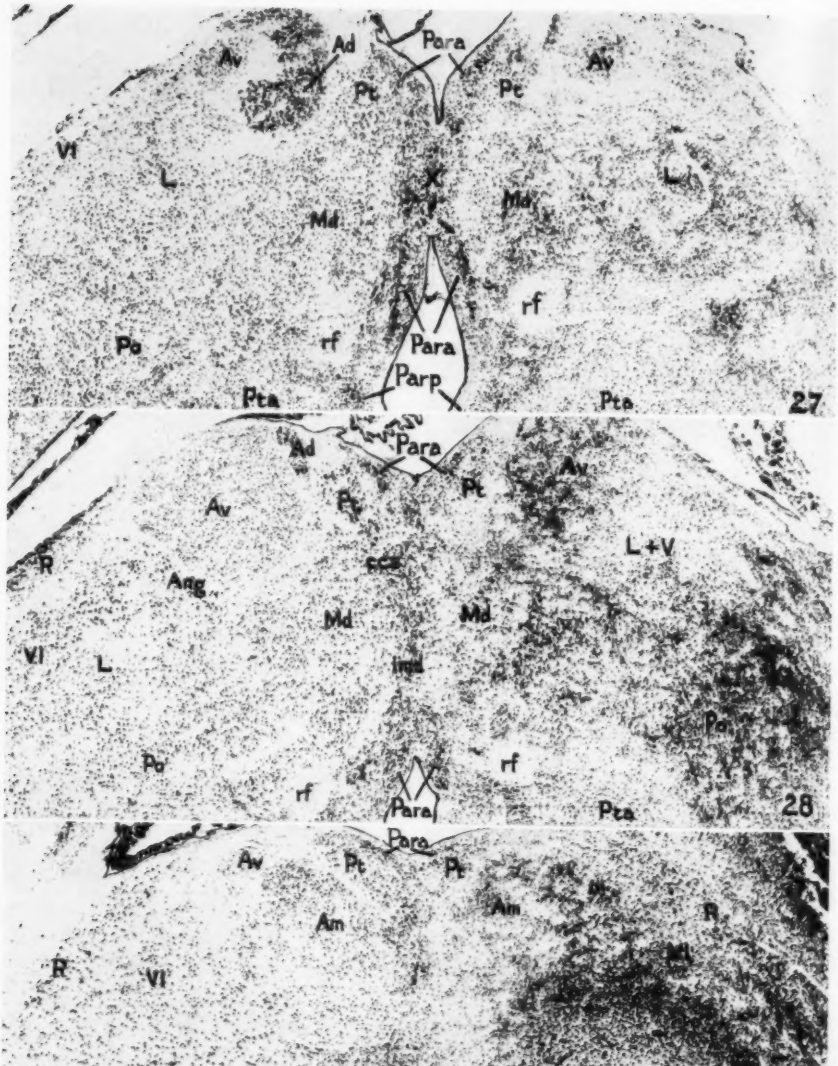
FIG. 25. Normal rabbit, × 30.

FIG. 26. RW 19, SECTION 460, × 30.

FIGS. 24 and 26 show areas outlined in Figs. 17 and 20. Fig. 25, from a normal rabbit, shows as closely as possible the region corresponding to that in Fig. 24. In Fig. 25 the central commissural system (ccs.) has not been cut quite symmetrically and the upper part of the figure does not correspond quite exactly with the region in Fig. 24.

Observe that all unpaired dorsal thalamic structures of the midline have disappeared on the left side in Figs. 24 and 26 and that the degeneration stops sharply along the midline. Note that ventral extremity of n. paraventricularis anterior (Para.) is not affected on the left in Fig. 24. The area designated as n. medioventralis (Mv.) in Figs. 24 and 25 is the fusion area between this element and n. parataenialis.

Am., n. anteromedialis; ccs., central commissural system; Cg., central gray; iam., n. interanteromedialis; Mv., n. medioventralis; Para., n. paraventricularis anterior; Va., n. ventroanterior.


Av
Ad
Para
Pt
Pc
Vl
L
X
Md
rf
Para
Parp
Pta
27
Ad
Para
Av
Pt
R
Arg
ccs
L+V
Md
Vl
L
ima
Po
rf
Para
Pta
28
Para
Av
Pt
Am
R
Vl
ccs
Var
rf
29

FIGS. 27–29

low power its sectors are not clear enough. However, under higher power one can differentiate within it the main pulvinar proper and pars geniculata pulvinaris adhering as a rim to the dorsal lateral geniculate body. The type of degeneration is probably different in these two sectors, because the pulvinar proper reacts with a slight glial proliferation whereas pars geniculata reacts very intensely. The dorsal lateral geniculate body, the ventral division of the medial geniculate and the whole ventral group react with very intense glial proliferation, which is least marked in the ventroanterior nucleus (Figs. 17–21). In addition the lateral and the posterior nuclei, as well as n. anterodorsalis and n. anteroventralis, react with intense gliosis, although not all the nuclei or sectors of them react entirely uniformly. Of course, it is not possible in cell preparations to delimit single elements from each other when they have degenerated completely. However, fiber sections often make it possible to recognize the boundaries of the elements with reasonable certainty. The normal cell pattern offers no simple anatomical suggestion which might explain the different forms of glial reaction seen. However, differences in the fiber content of the nuclei may be a relevant factor.

3. The ventral thalamus: While degeneration seems to follow an all or none principle in the dorsal thalamus and the epithalamus, this is

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FIG. 27. RW 10, SECTION 252, × 14.

FIG. 28. RW 10, SECTION 272, × 14.

FIG. 29. RW 10, SECTION 324, × 14.

These figures are also from horizontal sections. See Figs. 1 and 2 for locations of the sections and the extent of the operation. Reference to figures of RW 19 may help in further orientation. Fig. 27 corresponds to a level between Figs. 13 and 14, Fig. 28 to a level somewhat below Fig. 14 and Fig. 29 to a level somewhat below Fig. 16.

In Fig. 27 there is perhaps some loss of cells in the anterior group on the left resulting from a small cortical lesion on this side. The other nuclei on this side are quite normal in all figures. Note that all dorsal thalamic elements on the right are severely degenerated, but that the paraventricular complex (Para. and Parp.) and n. praetectalis anterior (Pta.), which is just visible in Figs. 27 and 28, are unchanged. Observe that, in the fusion area (X) in Fig. 27, some cells are lost on the right. Note, in Figs. 28 and 29, the severe degeneration of all midline structures on the right. Observe that in all degenerated elements there are more nerve cells present than in RW 19. Note particularly the great number of cells in the right reticular complex (R.) in Fig. 29.

Hl
Hm
Para
tth
Pt
ccs
lpt
Am
Mv
Hyp
Md
Vms
30
31
32

not so in the ventral thalamus of our demarcation. In the ventral thalamus we distinguish the reticular complex (R.), the complex of the ventral lateral geniculate body (Gev.) and the small suprahypothalamic group (Sh.). Figs. 14–20 show that the reticular complex has degenerated most severely. The complex of the ventral lateral geniculate body (Figs. 15–19) shows, even under low power, no change in the cells of any of its divisions, although some increase in glia probably has occurred. It is possible that with lesions of long standing the ventral lateral geniculate body might not remain entirely intact, but at 28 days after removal of the hemisphere it is clear that there are no demonstrable cell changes in this structure and it must be regarded, therefore, as independent of the telencephalon.

The behavior of the suprahypothalamic group (Sh., Fig. 20) is difficult to evaluate. This small group may be defined best as the area of fusion of the reticular complex with the hypothalamic nuclei. It is not easily separated in horizontal sections. It is fairly definite that marked gliosis has taken place in the suprahypothalamic group on the side of decortication and it is possible that there has been a decrease in the number of nerve cells, but, on the whole the suprahypothalamic group seems unchanged or very little affected by removal of the hemisphere.

4. Summary: In summary the following conclusion can be drawn

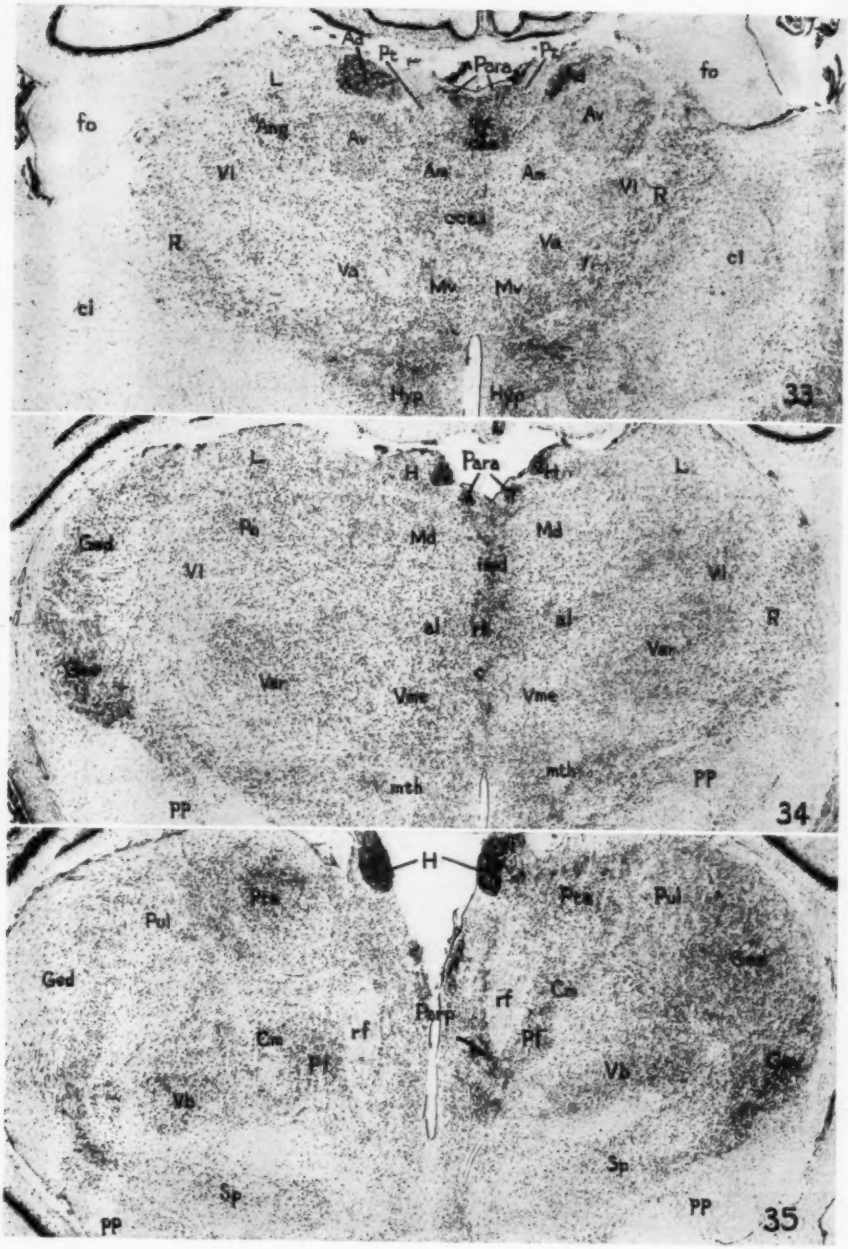
FIG. 30. RW 18, SECTION 884, × 30.

FIG. 31. RW 18, SECTION 912, × 30.

FIG. 32. RW 18, SECTION 1016, × 30.

These are frontal sections. Fig. 30 is most oral, Fig. 32 is most caudal. Observe in Fig. 30 the degeneration of n. parataenialis (Pt.) and of n. medioventralis (Mv.) on the right but the intactness of n. paraventricularis anterior (Para.). Note, in Figs. 31 and 32, that the latter element and the habenular complex are unchanged but that n. interparataenialis (ipt.), n. intermediodorsalis (imd.) and the rest of the midline dorsal thalamic structures are degenerated. Observe the slight glial reaction in these elements on the operated side and compare the normal cell pattern on the left with the glial reaction on the right in Fig. 32.

Am., n. anteromedialis; ccs., central commissural system; fo., fornix; Hl., n. habenularis lateralis; Hm., n. habenularis medialis; Hyp., hypothalamus; imd., n. intermediodorsalis; ipt., n. interparataenialis; Md., n. mediodorsalis; Mv., n. medioventralis; Para., n. paraventricularis anterior; Pt., n. parataenialis; tth., taenia thalami; Vme., pars medialis of the ventrabasal complex.


Pt
Para
fo
L
Ang
Av
VI
Am
R
Va
Mv
cl
Hyp
33
H
Md
Gad
Pa
fasc
al
Vm
Vme
mth
PP
34
Pca
Pul
Cau
rf
Pf
Vb
Sp
35

FIGS. 33–35

from these three experiments. *After removal of the telencephalon to the extent described above, the epithalamus (i.e., the paraventricular complex, the habenular complex and the pretectal group) remained unchanged; all dorsal thalamic nuclei degenerated and the degeneration did not spare any sector of any element; in the ventral thalamus the reticular complex degenerated, but the other ventral thalamic groups (the ventral lateral geniculate body and the suprahypothalamic group) were either unaffected or only slightly altered.*

*Degree of degeneration in relation to length of survival.* Before report-

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FIG. 33. RW 8, SECTION 924, × 10.

FIG. 34. RW 8, SECTION 992, × 10.

FIG. 35. RW 8, SECTION 1064, × 10.

See Figs. 7 and 8 for the extent of the operation in this animal and the location of the sections. Fig. 33 is most oral, Fig. 35 most caudal. Compare the normal cell pattern on the left with that on the right. Observe that n. parataenialis (Pt.) and its commissural system are intact on the right. Note also that n. intermediodorsalis (imd.) and the rhomboidal division (rh.) of the central commissural system with its wing (al.) show little or no change. Observe, further, that the midline structures between both anteromedial nuclei (Am.), as well as the central commissural system below them, in Fig. 33, and the central division (c.) of the central commissural system, in Fig. 34, show obvious changes on the right. Note lack of change in n. parafascicularis (Pf.) in Fig. 35. Observe that all other dorsal thalamic nuclei on the right are severely degenerated but that the anterodorsal element (Ad.) and n. mediodorsalis (Md.) have many cells. The right reticular complex (R.) shows many cells. The paraventricular and habenular complexes (Para., Parp. and Hl.) and the anterior pretectal nucleus (Pta.) are quite normal on the right.

Ad., n. anterodorsalis; al., wing of the rhomboidal division of the central commissural system; Am., n. anteromedialis; Ang., n. angularis; Av., n. anteroventralis; c., central division of the central commissural system; ccs., central commissural system; ci., capsula interna; Cm., centrum medianum; fo., fornix; Ged., corpus geniculatum laterale dorsale; Gev., corpus geniculatum laterale ventrale; H., habenular complex; imd., n. intermediodorsalis; ipt., n. interparataenialis; L., n. lateralis; Md., n. mediodorsalis; mth., fasciculus mamillothalamicus; Mv., n. medioventralis; Para., n. paraventricularis anterior; Parp., n. paraventricularis posterior; Pf., n. parafascicularis; Po., n. posterior; pp., pes pedunculi; Pta., n. praetectalis anterior; Pul., pulvinar; R., reticular complex; rf., fasciculus retroflexus Meynerti; rh., rhomboidal division of the central commissural system; sp., suprapeduncular complex of the subthalamus; Va., n. ventroanterior; Var., pars arcuata of the ventrobasal complex; Vb., ventrobasal complex; Vl., ventrolateral complex; Vme., pars medialis of the ventrobasal complex.

ing the extent of thalamic degeneration found in animals with less than the whole telencephalon ablated, some facts concerning the degree of degeneration in relation to the time at which the animal was sacrificed should be noted. Of the three rabbits described above, two were killed on the 28th day after operation, one on the 19th day. The changes, as already stated, were essentially identical in all three animals. However, in rabbit RW 10, which was permitted to live only 19 days, quite a number of rather well preserved cells were present throughout the degenerated thalamus, whereas in the other two animals the degeneration of the dorsal thalamic nuclei and of the reticular complex was extremely severe and there were practically no intact nerve cells present in any of the degenerated elements (cf. Figs. 27–29 of RW 10 with Figs. 10–21 and Figs. 30–32 of RW 19 and RW 18). Since, fortunately, the operation in RW 10 was the most extensive, the difference in the number of persisting cells in the thalami of these animals can be related only to differences in survival times. Figs. 27–29 show that the number of nerve cells in the degenerated thalamus of RW 10 is so small that there can be no doubt of the severity of the degeneration. The persisting cells, however, are not distributed uniformly throughout the thalamus. They are present in larger numbers in the midline nuclei and neighboring elements and also in n. anterodorsalis and in the reticular complex of the ventral thalamus. Were it not for the fact that all cells of these elements either completely disappeared or were very severely changed after 28 days (cf. Figs. 10–21), it would not be entirely clear from the 19 day preparation that these structures are entirely dependent on the telencephalon. It may be noted further that even after 28 days the different rates of degeneration in various elements may still be recognized by the number of incompletely degenerated cells still present. *Consequently, the presence of a large number of more or less intact cells in the midline nuclei and neighboring elements, in n. anterodorsalis and particularly in the reticular complex of animals surviving 18–19 days after removal of less than the whole telencephalon does not prove that the telencephalic centers on which these elements depend have been spared by the operation.* This conclusion is important for what follows, since all rabbits which will be described below were sacrificed 18–19 days after operation, except one which lived 22 days.

*B. Changes in the thalamus following partial ablation of the telencephalon*

*a. Changes following ablation of the whole cerebral cortex except for the cortex overlying subcortical telencephalic centers.* From the experiments reported above it is evident that all dorsal thalamic nuclei, probably without exception, are telencephalic dependencies, *i.e.*, they depend either on cortex or on subcortical telencephalic centers or on both. It is well known that many dorsal thalamic elements are cortical dependencies, but is there also a group of striatal dependencies in the dorsal thalamus? As mentioned in the introduction, removal of all cortex without causing serious injuries to subcortical telencephalic centers is a most difficult problem technically and in the small, soft brain of the rabbit possibly a hopeless task. Therefore, the procedure adopted was to ablate only as much of the cortex as practicable without causing any essential injury to subcortical telencephalic centers. Such an operation may not provide a conclusive answer regarding the existence of striatal dependencies in the dorsal thalamus, but it can eliminate those thalamic elements which are not striatal dependencies and it can delimit the largest possible extent of the dorsal thalamic group which may conceivably depend on striatum or amygdala.

*Description of ablations in RW 8 and RW 6:* This type of operation was performed on two animals. In rabbit RW 6 the aim was to leave intact striatum and amygdala but to remove as much of the cortex as possible. In rabbit RW 8, on the other hand, the goal was to remove only neocortex in the strict sense and the limbic cortex (mesocortex of M. Rose, his regio infraradiata sive limbica and regio retrosplenialis) and to spare entirely all those cortical structures which it was necessary to spare partly in any case if serious injuries to striatum and amygdala were to be avoided. Figs. 5, 6, 7 and 8 show the extents of these two operations.

In RW 6 (Figs. 5 and 6) the striatum did not remain entirely uninjured. Some damage was done to its lateral margin and particularly to its oroventral end. However, comparison with the other side shows that the bulk of the striatum, as well as the whole amygdaloid complex, was preserved. In addition the following portions of the telencephalon remained on the operated side: 1. small fragments of the limbic region (Li.) and taenia tecta (tt.); 2. tuberculum olfactorium (Tol.) to a very large extent; 3. a rather large sector of the prepyriform region (Prpy.);

4. the whole periamygdaloid region (Pam.); 5. most of the entorhinal region (En.); 7. fragments of the presubicular region (Presub.) and of Ammon's formation (FA.); 8. septum (s.p.).

In RW 8 (Figs. 7 and 8) striatum and amygdala were practically intact. Some slight injury was done the most oroventral part of the former, and here and there the lateral border of the striatum just touches the lesion. In addition the following portions of the telencephalon remained on the operated side: 1. olfactory bulb (Bol.); 2. retrobulbar area (Rb.) almost undamaged; 3. nearly the whole prepyriform region (Prpy.); 4. whole tuberculum olfactorium (Tol.); 5. whole periamygdaloid region (Pam.); 6. whole entorhinal region (En.) with perirhinal fields (Prh.); 7. all of Ammon's formation (FA.) with fornix; 8. most of taenia tecta (tt.); 9. most of the presubicular region (Presub.); 10. all of the septal area (s.p.); 11. fragments of limbic cortex (limbic and retrosplenial regions, Li. and Rs.); 12. fragments of insular cortex (I.); and, finally, 13. large parts of the temporal region (T.) of the neocortex in the strict sense. It should be noted that the remaining fragments of limbic cortex and presubicular region show distinct atrophy in this animal.

The thalamus of RW 8 was not injured during operation. In the thalamus of RW 6 a superficial bruise, extending for a few sections, is present at the level of section 1020 (Fig. 5). Moreover, another microscopical and quite superficial laceration is present behind the level of section 1080 for a few sections. No injury was done to hypothalamus or midbrain in either animal.

*Description of findings in RW 8 and RW 6:* With one exception, the findings in the thalamus are not very different in these two brains. It is convenient to start with some general remarks. First it may be noted that the character of the degeneration is somewhat different with these limited operations than when the whole telencephalon is removed. A somewhat larger number of nerve cells persists in the degenerated elements and it is evident that the persistent nerve cells (after 19 days) are more normal. It is, however, neither the larger number of nerve cells, nor their more normal appearance which seems to make the main difference in the degenerated elements. It is obviously the glial reaction. With complete ablation of the telencephalon there are, as was pointed out, many elements which react with very intense gliosis.

With the more limited ablations glial proliferation is generally much less pronounced, although the differences in reaction types among the various nuclei are still present. In our limited ablations of the cortex some elements of the dorsal thalamus are, as will be shown, unchanged or only slightly altered. With this there seems to be associated the fact that, at least in some severely degenerated elements bordering the unchanged nuclei, a larger number of cells is found at the border regions than would be expected from the average cell count in other degenerated elements. There are several possibilities to account for this fact. The simplest is that the whole projection area for the element was not destroyed or that the anatomical delimitation of the thalamic element requires reconsideration. Until these possibilities are excluded one cannot suggest that the intactness of some thalamic elements may aid in the preservation of other thalamic structures. However, we shall not comment further on this problem here.

In RW 8 (and in RW 6) all epithalamic elements of our demarcation are, of course, entirely intact. In order to avoid repetition, it may be stated at once that the whole epithalamus remained unchanged in all other experiments.

In regard to the ventral thalamus, RW 8 and RW 6 yield little new information. The ventral lateral geniculate body, of course, is intact (Fig. 35). The suprahypothalamic group shows questionable changes. The reticular complex (R. in Figs. 33 and 34) exhibits undoubted signs of degeneration but possesses a very large number of excellently preserved cells. It has been pointed out that 19 days after removal of the whole telencephalon there are many cells still present in this complex, which after 28 days, have degenerated. There is little doubt that after more limited ablations the reticular complex on the whole is better preserved than after total ablations of the hemisphere. However, the glial reaction in the reticular complex is less severe with limited than with total ablations and it appears to be related to the rate at which degeneration proceeds. It is apparent, then, that our material is inadequate to prove whether preservation of subcortical telencephalic centers has any influence on the behavior of the reticular complex. Therefore, we shall not comment further on changes in this complex in experiments yet to be described.

In the dorsal thalamus of RW 8 all elements of the anterior, ventral

and dorsolateral groups, as well as the dorsal lateral geniculate body, are degenerated severely (Figs. 33–35). In the anterior group of nuclei there are numerous cells in the anterodorsal element and quite a few also in the most anterior part of the anteromedial nucleus. Because most of the latter element is severely degenerated, this strongly suggests that the remnants of the limbic fields account for the preservation of cells in its anterior fraction. In regard to the anterodorsal element, persistence of some of its cells should be expected in accord with our remarks on p. 104. However, there is no doubt that severe degeneration has occurred in this element. We shall not further mention the fact that in some sectors of the anterodorsal element many cells still persist in all animals 19 days after operation.

The dorsal division of the medial geniculate body is almost entirely intact; the ventral division is degenerated except for its lateral caudal portion. There can be little doubt that this partial preservation of the medial geniculate body resulted from the presence of large portions of the temporal region.

Somewhat more difficult to evaluate is the behavior of the medial group. N. mediodorsalis and n. medioventralis are essentially degenerated (Figs. 33 and 34), although they contain more cells than other degenerated elements, particularly in certain sectors. N. parataenialis and n. interparataenialis are quite intact (Fig. 33). Also intact, or nearly so, are n. intermediodorsalis and the rhomboidal division of the central commissural system (n. rhomboidalis) with its wing curving around the parataenial and the mediodorsal nuclei (Figs. 33 and 34). This wing may correspond (but, if so, probably only partly) to n. paracentralis and n. centralis lateralis in other mammals. It is noteworthy that other midline structures are not intact (Figs. 33 and 34). There are rather obvious changes in n. interanteromedialis, in the central division of the central commissural system (n. centralis, Fig. 34) and in the commissural system of the ventral group, although many cells are still present in these formations. The last group which is intact, or nearly so, is the postmedial group consisting of n. parafascicularis and centrum medianum. N. parafascicularis is undoubtedly well preserved (Fig. 35) but evaluation of centrum medianum is difficult. There may be some changes in the latter but on the whole the area seems well preserved.

In the dorsal thalamus of RW 6 all elements of the anterior, ventral and the dorsolateral groups (*i.e.*, n. anterodorsalis, n. anteromedialis, n. anteroventralis, n. ventroanterior, the ventrolateral complex, the ventrobasal complex, the magnocellular or angular nucleus, n. lateralis, n. posterior and the pulvinar complex), as well as the dorsal lateral geniculate body and both divisions of the medial geniculate, have degenerated in their whole extent. The only element which contains many well preserved cells is, of course, n. anterodorsalis. In the medial group there is severe degeneration of n. mediodorsalis and of n. medioventralis. Evaluation of degeneration in the latter, however, is difficult since this nucleus is probably not intact on the "normal" side. Of the midline structures, n. interanteromedialis, the central division of the central commissural system and the commissural system of the ventral group show degenerative changes similar to those seen in RW 8, although many cells are well preserved. N. parafascicularis is either intact or only slightly changed. Centrum medianum is still more difficult to evaluate than in RW 8. On the whole it seems to be well preserved but its cells may be shrunken and less numerous than normal. N. parataenialis, n. interparataenialis, n. intermediodorsalis and the rhomboidal part of the central commissural system with its wing, which are practically intact in RW 8, do not appear to be entirely intact in RW 6. However, all these structures contain so many excellently preserved cells that they must be classified as very little changed. Of all these structures n. parataenialis and n. interparataenialis are best preserved, the wing of the rhomboidal division of the central commissural system least.

*Summary: The findings in these two animals demonstrate that all the major elements of the dorsal thalamus of the rabbit are cortical dependencies. There are only a few elements which conceivably can depend on striatum or amygdala. These elements are n. parafascicularis, centrum medianum, n. parataenialis with its commissural system, n. intermediodorsalis and the rhomboidal division of the central commissural system with its wing. It is obvious, of course, that all these structures may depend on those parts of the cortex which were not removed in these experiments or on both cortex and subcortical telencephalic centers.* In listing all the structures enumerated above as possible striatal dependencies, a conservative estimate is offered, since we regard the demonstrable changes in

these structures in RW 6 as inconclusive both because these changes are minor and because the striatum was not entirely intact in this animal. To what extent comparative anatomical facts and the experimental evidence suggest considering these structures as cortical or striatal dependencies will be dealt with in some detail in the discussion.

*b. Changes following subtotal ablation of cortex and subcortical telencephalic centers.* In order to produce degeneration in some, but not all, of the dorsal thalamic elements which were intact or nearly so in RW 8 and RW 6, an ablation more extensive than RW 6 but less than total unilateral removal of the telencephalon is necessary. But since such an operation is bound to cause injury to the striatum, it cannot prove conclusively whether the dorsal thalamic elements in question depend on cortex or subcortical centers. However, it can define more closely which cortical areas and which portions of the subcortical centers are to be taken into consideration as projection areas for some of the dorsal thalamic elements listed as possible striatal dependencies.

*Description of ablation in RW 12:* Subtotal removal of the telencephalon was effected in one animal (RW 12). In two others (RW 9 and RW 30), although the goal of the operation was different, the actual damage produced effects in the thalamus nearly identical with the effects of subtotal ablation. The aim of the operation in RW 12 was to remove all the telencephalon except the septum and the olfactory tubercle, leaving those portions of the subcortical centers which lie between the olfactory tubercle and the diencephalon. The operation was a limited success. Fig. 9 shows its extent. Of the telencephalic structures which should have been removed, there remained: 1. fragments of the amygdaloid nuclei (Am.); 2. fragments of periamygdaloid region (Pam.); 3. remnants of Ammon's formation (FA.); 4. negligible traces of entorhinal region; 5. a few cells of taenia tecta. The parts of amygdala which remain probably are not larger than in the attempted total ablations. The periamygdaloid cortex has been largely destroyed. There are no remnants of retrobulbar, prepyriform or presubicular regions. The striatum has been destroyed almost completely except for its oroventral portion. The globus pallidus (P.) and area diagonalis (Diag.) are present practically entirely. The rest of the hypothalamus is uninjured. The telencephalic structures, which were to be left intact, however, are also injured. The septum (s.p.) is for

the most part not involved in the lesion, but it shows for some distance a small area of softening. The tuberculum olfactorium, on the other hand, is considerably injured. On the normal side it extends approximately from section 528 to section 760, on the operated side from section 600 to section 720. A considerable sector of it, therefore, is preserved. When present it borders the lesion laterally. The thalamus was not injured during operation except for a tiny superficial bruise in the dorsal layers of the optic tract for a few sections between 1020 and 1092 (Fig. 9).

*Description of findings in RW 12:* The changes in the thalamus of RW 12 are very similar to those seen after total ablation of the telencephalon in a 19 day preparation with one significant exception. The anterior, ventral and dorsolateral nuclear groups, as well as the dorsal lateral geniculate and the dorsal and ventral divisions of the medial geniculate are degenerated, as in RW 10. Likewise, n. mediodorsalis and n. medioventralis are severely degenerated. In n. medioventralis numerous cells persist and their number is not greatly less than in this element on the other side. There is little doubt, however, that n. medioventralis on the other side is degenerated also—the result of a lesion in the other hemisphere not shown in Fig. 9. In the group of dorsal thalamic nuclei which degenerated in RW 10, RW 18 and RW 19, but were found intact or nearly so in RW 6 and RW 8, the findings are as follows: N. parafascicularis and centrum medianum are degenerated completely. The rhomboidal division of the central commissural system with its wing, as well as other portions of this system, also are very severely degenerated. N. intermediodorsalis on the whole probably contains more cells than it does in the total ablation, particularly in its caudal portions, but there is no doubt that it is severely affected. On the other hand n. parataenialis and n. interparataenialis are on the whole well preserved, although this system, too, is not intact and shows a marked loss of cells, particularly in the caudal portions and along the lateral margin of the parataenial nucleus. There are very few telencephalic structures which can be held responsible for this relatively excellent preservation of the parataenial and interparataenial nuclei. They are the septum, the remaining portions of the tuberculum olfactorium and the remaining portions of the striatum. Perhaps the remnants of the amygdala also should be considered.

*This experiment on subtotal ablation shows plainly how even small fragments of relevant portions of the telencephalon may influence the behavior of the midline nuclei of the dorsal thalamus. Yet the operation in RW 12 was more extensive than most experiments on removal of the endbrain reported in the literature.*

*Description of ablations in RW 9 and RW 30*: In RW 9 the aim was to leave the limbic cortex with its connections but to destroy the rest of the cortex. The purpose in RW 30 was to remove only the insular cortex and the prepyriform region. The operations, however, were not successful and it seems superfluous to list all the structures which were left because in both cases areas of softening and infiltration developed which destroyed almost all of the striatum except for its oroventral parts and interrupted all lateral thalamic radiations. The anterior thalamic radiations were in both cases partly preserved. The septum was not damaged in either case and the tuberculum olfactorium was partly preserved in RW 9 and largely so in RW 30. Furthermore, Ammon's formation and the fornix were intact in RW 30, but largely destroyed in RW 9. Finally, in both animals the periamygdaloid region was almost completely destroyed and only small fragments of the amygdaloid nuclei remained. The diagonal area was nearly completely intact in both animals. Globus pallidus was largely preserved in RW 9, mostly destroyed in RW 30. The rest of the hypothalamus was normal in both preparations. In the thalamus of RW 9 direct injury was done to the anterior tubercle and a very small injury to the ventral thalamus. Otherwise the thalami of both animals show only secondary changes. RW 9 was killed 18 days, and RW 30 22 days after operation.

*Description of findings in RW 9 and RW 30:* In the dorsal thalamus of each of these animals the changes are very similar to those seen after subtotal ablation in RW 12. All the main dorsal thalamic nuclei are degenerated, as in RW 12, but some differences exist. The most important is the obviously good preservation of n. medioventralis particularly in its anterior portion in RW 30. Of the group characterized above as possible striatal dependencies, n. parafascicularis and centrum medianum are degenerated completely. The same, on the whole, is true for the rhomboidal division of the central commissural system and its wing. N. intermediodorsalis clearly is affected, although it

contains many cells. N. parataenialis and n. interparataenialis are intact anteriorly and slightly changed posteriorly in RW 30. These nuclei are best preserved of all the dorsal thalamic structures in RW 9 but they are not entirely intact.

## DISCUSSION

### *A. The epithalamus*

The experiments here reported show that the epithalamus of our demarcation (*i.e.*, the habenular complex, the paraventricular complex and the pretectal group) remains unaffected by removal of the whole cerebral cortex and, indeed, it appears to be entirely independent of the telencephalon. The latter statement, however, requires qualification, since even in the most extensive of our operations (RW 10), where one can speak of a very satisfactory ablation of the telencephalon, minute fragments of it still remained. It appears well nigh impossible that these minute fragments could have preserved the whole large epithalamic group, but, though unlikely, it is conceivable that they (particularly the fragments of amygdala) had some influence on the preservation of some epithalamic elements. It has been pointed out elsewhere (J. E. Rose, 1942a and b) that this behavior of the epithalamus is in very good agreement with embryological and comparative anatomical considerations.

Our findings in regard to the epithalamus are in complete agreement with those of Nissl (1913), Brouwer (1920), von Monakow (1925), Schaltenbrand and Cobb (1931), Bard and Rioch (1937) and virtually all other investigators, provided these nuclei are mentioned at all by them. However, the value of this general agreement is considerably limited by the fact that with most workers the animals usually showed large portions of both cortex and subcortical telencephalic centers left during operation.

Of great interest is the problem of cortical connections of the epithalamic nuclei. Most observers agree that the habenular complex has cortical connections. However, only corticifugal fibers are generally conceded (Kappers, Huber and Crosby, 1936). In regard to the pretectal group, Clark (1932) presented evidence that the pretectal nucleus of the rat (identical probably with n. praetectalis anterior of our demarcation) receives cortical fibers but he suggested that it does not send

any fibers to the cortex. On the other hand, Papez and Freeman (1930) state that the pretectal nucleus of the rat gives off corticipetal fibers. Although it is likely that the pretectal nucleus of these authors also includes dorsal thalamic elements, their statement that the nucleus of the posterior commissure also sends fibers to the cortex makes it clear that pretectal elements of our designation also were meant. If the opinion of Papez and Freeman should be confirmed, it would follow that not every thalamic element with corticipetal connections is necessarily a cortical dependency.

Because of the confusion it causes among students of the auditory system of the rabbit, n. supragenículatus praetectalis is of considerable practical interest. This element was delimited by Münzer and Wiener (1902) as n. supragenículatus because it did not degenerate after ablation of the cortex. Later Nissl proved conclusively that it is entirely independent of the whole cortex, auditory cortex included. Unfortunately, however, Winkler and Potter (1911) included this element in the medial geniculate body and most authors have followed their authority. Hence, through inclusion of this nucleus, probably together with n. tracti optici, in the medial geniculate, frequent statements that the dorsal division of the medial geniculate body is independent of the cortex have resulted. It is, of course, a matter of definition whether one includes n. supragenículatus praetectalis in the medial geniculate. We think it is less confusing not to do so despite its close topographical relation to the medial geniculate body, a relationship which suggests that this element may play some role in the auditory performance of the animal. The prodigious development of this nucleus in the rabbit suggests that it may be related to movements of the ear.

### *B. The dorsal thalamus*

In contrast with the epithalamus, all dorsal thalamic elements, without exception, are telencephalic dependencies. This statement is limited only by the fact that in the total ablations of the telencephalon both the diagonal area and the globus pallidus, both of which we regard as hypothalamic structures, also were injured. However, in one experiment at least (RW 19), the globus pallidus largely was not involved and in the subtotal ablation (RW 12) the diagonal area and the globus pallidus practically were uninjured. These facts indicate that the only

dorsal thalamic elements which can possibly depend on these structures are the parataenial nucleus and its commissural system. It seems fair, however, to exclude this possibility, first, because in the total ablation experiments degeneration of the parataenial nucleus and its commissural system were not at all correlated with the amount of diagonal area and globus pallidus destroyed and, secondly, because comparative anatomical facts are not compatible with such an assumption. Finally it may be mentioned that in RW 30 the parataenial and interparataenial nuclei were little or not at all altered despite the very considerable destruction of the globus pallidus. In regard to area diagonalis, it will be noted below, that this structure itself does not remain intact after ablation of the telencephalon and thus it appears still less probable that any thalamic element depends on it.

Our finding, that all dorsal thalamic elements are telencephalic dependencies, is in perfect agreement with Nissl's (1913) observations but differs considerably from the conclusions of most other authors. This is to be expected, since, except for some older reports, complete ablation of the telencephalon has been performed only exceptionally and because most experimenters have tried to remove only the neocortex and the limbic fields leaving the pyriform lobe and the subcortical telencephalic centers. Strangely enough, however, it is generally assumed that a specimen deprived of its limbic cortex and neocortex represents a completely decorticated preparation and the possibility, indeed probability, that the so-called olfactory fields may be responsible for preservation of some dorsal thalamic elements usually is entirely ignored.

Since all dorsal thalamic elements depend on the telencephalon, it is necessary to consider how many of them are cortical dependencies and whether there is sufficient evidence to assume that there exists a dorsal thalamic group which depends on striatum or amygdala.

*a. Dorsal thalamic elements which are cortical dependencies.* The experiments in which the subcortical telencephalic centers were either intact or only slightly injured have shown that all major dorsal thalamic elements are essentially cortical dependencies only. These elements are the anterior, the ventral and the dorsolateral groups, the dorsal lateral and the medial geniculate bodies, some elements of the medial group and some nuclei of the midline.

In the rabbit the anterior group consists of the anteroventral, the

anterodorsal and the anteromedial nuclei. In recent years overwhelming evidence has accumulated that all these elements project to the cortex (Clark and Boggon, 1933a and b; Lashley, 1941; Papez, 1938; Walker, 1938a and b; Waller, 1934, 1937, 1938). It has been pointed out in the description of results that in the rabbit the anterodorsal nucleus shows severe changes in all its cells only after 4 weeks following removal of the whole telencephalon, whereas at 19 days many of its cells are either intact or only slightly changed. Hence, it is obvious that the presence of many cells in this element in animals with short survival periods does not prove that its projection area was spared. If the cells of the anterodorsal nucleus of the cat behave similarly to those in the rabbit, Waller's (1938) suggestion, that this element has prominent subcortical connections, lacks experimental foundation, because none of his animals survived longer than 2 weeks. However, we do not yet possess specimens from animals without subcortical telencephalic injury and with long survival periods which might definitely determine whether the anterodorsal nucleus lacks subcortical connections.

All elements of the ventral group of the rabbit, *i.e.*, n. ventroanterior, the ventrobasal complex, the ventrolateral complex and the angular or magnocellular nucleus, depend on the cortex. There is rather general agreement on this point, although some observers report that single ventral elements or parts of them are spared in their experiments (Papez, 1938; Walker, 1938a and b). However, the fact, that various portions of the ventral group are reported as intact, seems to indicate that the differences are due to incomplete cortical ablations.

All elements of the dorsolateral group, *i.e.*, the lateral and the posterior nuclei and the pulvinar group, also are undoubtedly dependent on the cortex. In higher mammals, most writers agree on this, but Lashley (1941) stated that a posterior portion of the lateral nucleus was intact in his specimen of decorticated rat. We assume that this difference arises from confusion of the dorsolateral group with pretectal elements in the rat thalamus rather than from actual difference in results.

That the dorsal lateral geniculate body and the medial geniculate are cortical dependencies is seldom contested in higher mammals. In the rodent thalamus, however, and particularly in the rabbit, inclusion of

some pretectal elements in the medial geniculate has resulted, as already mentioned, in contradictory statements about the dorsal division of the medial geniculate. This seems to apply to the statement of Lashley (1941) about the behavior of the medial geniculate after hemidecortication of the rat. On the other hand, partial preservation of the medial geniculate in the opossum (Bodian, 1942) seems best explained if the temporal fields which remained, were not as completely undercut as Bodian believed them to be (cf. our RW 8).

In the medial group n. mediodorsalis and n. medioventralis are, we believe, entirely dependent on the cortex. However, our delimitation of n. mediodorsalis may be somewhat different from that of other authors. With respect to this nucleus there is general agreement among more recent authors that it is dependent on the cortex. This is not so for n. medioventralis. In n. medioventralis we include, for the time being, n. medialis ventralis of M. Rose (1935) and his n. inframedialis (n. paramedianus of some authors); both portions are rather well separable in the rabbit. N. medioventralis probably corresponds largely to n. reuniens of most authors. Clark and Boggon (1933b) and Waller (1938, 1940) found changes in n. reuniens of rat and cat but, since striatal injuries were present, they cautiously did not attribute them to cortical lesions. Lashley (1941), however, found n. reuniens degenerated, without injury to the striatum in the rat. Stoffels (1939a) concluded that n. paramedianus projects to the cortex in the rabbit. We are the more positive about the dependence of n. medioventralis on the cortex, because we have found severe degeneration of this nucleus not only in RW 6 and RW 8 but also definite changes in this element in the thalamus of the other side in a number of animals in which there were cortical lesions of the remaining hemispheres without subcortical injury. Finally, we possess other brains with small lesions restricted to the cortex in which there are changes in n. medioventralis.

Quite in disagreement with most authors is our finding that the following structures do not remain intact after lesions confined to the cortex: n. interanteromedialis, the simple commissural fusion between both nn. medioventrales, the central division of the central commissural system with its wing (probably corresponding to n. centralis medialis and to parts of n. paracentralis and n. centralis lateralis), and the

commissural system between the ventral nuclei. It may be conceded that the changes after 19 days are not very impressive but they are, nevertheless, sufficiently marked that they cannot be ignored. That these nuclei failed to degenerate completely in RW 6 and RW 8 after 19 days is not surprising, since in the total ablation experiments they did not degenerate completely within this period. The number of cells remaining in these nuclei is rather large and this suggests that their projection areas were not entirely destroyed. Since injury to subcortical centers was negligible in these experiments and since the changes in the nuclei were well marked, it is logical to assume that, if parts of the projection areas remained, these were in all likelihood cortical areas. We shall return to this point below.

*b. Dorsal thalamic elements which may depend on cerebral cortex, on subcortical telencephalic centers or on both.* Comparison of the experiments on total and subtotal ablations of the telencephalon with those in which subcortical telencephalic centers remained intact shows that degeneration is more extensive in the former. Hence, those thalamic nuclei, which degenerate in the first type of experiment but remain intact in the second, may depend either on subcortical telencephalic centers or on those portions of cerebral cortex which remained in the second type, or, finally, on both subcortical and cortical structures. The elements in question are: n. parataenialis, n. interparataenialis,[3] the rhomboidal division of the central commissural system (probably corresponding to n. rhomboidalis and to parts of n. centralis lateralis and n. paracentralis), n. intermediodorsalis and the postmedial group consisting of n. parafascicularis and centrum medianum.

Our observation that all dorsal thalamic nuclei of the midline degenerate after ablation of the telencephalon is in agreement with Nissl's (1913) findings but contrary to the results of most other authors, who apparently assume that the midline and intralaminar structures remain essentially unaffected after all telencephalic lesions. However, in spite of this generally accepted view, some experimenters have noted that with extensive lesions of the telencephalon some changes in these struc-

[3] Experiment RW 12 leaves open the question whether the septal structures are relevant to the preservation of the parataenial and interparataenial nuclei. However, the septal structures themselves do not remain intact after destruction of the rest of the telecephalon (see p. 123).

tures do occur. The elements found affected most frequently are n. paracentralis and n. centralis lateralis, but Bard and Rioch (1937) pointed out that the midline group also showed changes in their preparations. From Rothmann's (1923) and Morrison's (1928) descriptions, it is evident that they also found the dorsal thalamic midline structures altered. It is clear that those whose experiments approached total ablation of the telencephalon found changes in the midline group, whereas those who denied such changes left considerable portions of the rhinencephalon and parts of the subcortical centers intact. These authors paid little attention to changes in the midline group, apparently because severe damage always was done to the thalamus itself. Since in our experiments the thalamus was not injured directly, the conclusion appears warranted that *total ablation of the telencephalon, without injury to the hypothalamus, produces degeneration in the midline nuclei, which after 4 weeks is as severe as in other dorsal thalamic elements.*

The evidence that the midline nuclei are telencephalic dependencies leaves open the question whether they depend on cortex or on subcortical telencephalic centers. It has been pointed out above that intactness of the subcortical centers can be assured only if considerable portions of the so-called olfactory cortex are left. If the amygdala is neglected, then, despite the fact that the evidence offered is not conclusive, several facts may be mentioned which indicate that all the dorsal thalamic elements under consideration probably depend on remaining cortex rather than on caudate and putamen. It is convenient to discuss the midline nuclei in two groups: (1) n. parataenialis, n. interparataenialis, the rhomboidal division of the central commissural system with its wing and n. intermediodorsalis; (2) the postmedial group which includes centrum medianum and n. parafascicularis.

In regard to the first of these groups it may be repeated that minor changes were observed in RW 6. It is true that the striatum in this animal was not entirely intact. However to assume that these changes were due to minor injuries of the striatum would postulate that the midline nuclei are very vulnerable to any injury of the striatum. This obviously is not so, because in other mammals most authors have failed to observe such changes even with very considerable damage to the striatum. The behavior of the whole midline group in phylogeny is of

great interest. The fact that it undergoes great reduction, at least relatively, in higher mammals and particularly in primates would be difficult to explain if this group depends on the striatum, since there is no evidence that the striatum becomes reduced in higher mammals. On the other hand, if this whole group depends mainly on the so-called olfactory fields, its relative reduction in the primate thalamus would be reasonable. A further suggestion that the striatum is not likely to play a role in the preservation of this group was made by Waller (1938). He stated that, in a large series of lesions placed in various parts of the striatum with the Horsley-Clarke apparatus, he found it exceedingly difficult to produce cell reaction in the dorsal thalamus. Finally, some authors report degeneration in the parataenial nucleus after cortical lesions in olfactory fields. Stoffels (1939b) maintains and Lashley (1941) agrees that this nucleus projects to the retrobulbar area and taenia tecta. Our experiments do not favor this view although they are not incompatible with it. The parataenial nucleus was quite intact in RW 8 in which the retrobulbar area was undamaged, but it was also preserved to a very considerable extent, but not intact, in RW 6 and RW 12 in which not a trace of retrobulbar area remained. RW 12 and RW 9 suggest, rather, that, if the parataenial nucleus depends on cortex, the relevant area, at least for preservation of its anterior portion, may be the tuberculum olfactorium. Stoffels offered no experiments in which the anterior portion of the parataenial nucleus was changed. His suggestion that taenia tecta is the projection area for this nucleus seems to have been an indirect conclusion only. Our experiments, which were not designed for localization of projection areas, are not conclusive, since we possess no animals with isolated lesions in the tuberculum olfactorium, nor any with the tuberculum olfactorium intact and the adjoining areas destroyed.

On what telencephalic centers n. parafascicularis and centrum medianum depend is a puzzling question. Centrum medianum of our demarcation is in the rabbit a small, indistinct area blended with n. parafascicularis. Its homology with centrum medianum of carnivores as defined by Rioch (1931) and by Ingram, Hannett and Ranson (1932) seems fairly certain. Whether, however, this area can be homologized with centrum medianum of primates is still somewhat uncertain, and it seems best to leave this question open until the projection area of

centrum medianum is known exactly in all these forms. Our experiments are not suited to determining the projection area of any element. If, however, it be true that centrum medianum arises in close connection with n. parafascicularis and if both project to neighboring areas and if our interpretation of its doubtful preservation in RW 6 and RW 8 is correct, then, cortical areas in proximity to the rhinal sulcus are likely projection areas for the postmedial group. The possibility that the postmedial group projects to other cortical areas remaining in RW 6 and RW 8 or to the striatum cannot be excluded, of course, although the expansion of the centrum medianum in primates and the minute dimensions of the more or less constant n. parafascicularis seem not to favor the striatum as the probable projection area. Clark and Russell (1939) have suggested that the centrum medianum may project to the insular cortex in man, but were unable to confirm this in monkey. Stoffels (1939a) stated that n. parafascicularis projects to the insular agranular cortex. Rabbit RW 6 makes it improbable that any other "neocortical" field than the most ventral portion of the insular region can be the projection area for the centrum medianum. It remains to determine whether isolated lesions in this region or in the adjoining prepyriform fields will cause any changes in the postmedial group. In any case the suggestion of Walker (1938b) that centrum medianum depends on globus pallidus and that of Waller (1938) that n. parafascicularis depends on hypothalamus are incompatible with our findings, because the whole postmedial group can be brought to complete degeneration without damage to the structures mentioned.

The cells in the dorsal thalamus which survive total ablation of the telencephalon are of considerable interest. It is usually stated that following hemidecortication two types of neuron are seen in the dorsal thalamus, those which are slightly or not at all changed (mainly nuclei of the midline) and those which are severely altered but have not completely disappeared even after long survivals (scattered cells in otherwise degenerated elements). There is no doubt that 4 weeks after complete ablation of the telencephalon of the rabbit there are practically no intact or unchanged cells in any sector of any dorsal thalmic element. Hence, the only experimental evidence for an intercalated cell system is the presence of distinctly altered cells scattered through otherwise completely degenerated nuclei. Furthermore, the number

of these cells persisting after 4 weeks is quite small and it remains to be seen whether with complete ablation of the telencephalon they will persist for any considerable length of time. However, even if all nerve cells should disappear from the dorsal thalamus, the existence of intercalated cell systems would be difficult to deny if one assumes (as is necessary in any case) that transneuronal changes take place very early in the dorsal thalamus and are already demonstrable after about 3 weeks[4].

*In summary, then, the following can be said about the dorsal thalamus: All dorsal thalamic nuclei are telencephalic dependencies; most of them are cortical dependencies, and only a small group can conceivably depend on striatum or amygdala. Even this group probably depends on cortex rather than on subcortical centers.*

If it be true that the dorsal thalamus is entirely dependent on cortex, the current belief that its nuclei project only to "neocortex" will have to be revised. As a matter of fact, this common view is incorrect in any case, since there is no doubt that the anterior group projects to the limbic cortex. To include the limbic cortex in the six layered neocortex, however, is arbitrary and hardly compatible with any morphological consideration. It is of paramount interest to establish whether other types of cortex than neocortex in the strict sense and limbic cortex receive projection fibers from the dorsal thalamus. It is still uncertain whether the insular cortex, the pyriform cortex (schizocortex

[4] The occurrence of transneuronal changes in the thalamus and the possibility of confusing them with retrograde changes are still matters of conjecture. It is well known that destruction of the optic tract does not cause (even after many months) changes in the dorsal lateral geniculate body comparable to those seen within 2 to 4 weeks after destruction of the visual cortex. The same is true for changes which occur in certain nuclei of the mamillary complex of the adult rabbit after destruction of the cortex on which the anterior nuclear group of the dorsal thalamus depends. Four weeks after total ablation of the telencephalon, changes in the mamillary nuclei are rather slight and cannot be confused with the severe retrograde degeneration of these nuclei which follows destruction of the anterior nuclear group. However, it has long been known that ablation, in the new born rabbit, of the cortex, on which the anterior group depends, without injury to the thalamus, causes certain mamillary nuclei to disappear completely after a few weeks. This indicates that under certain conditions transneuronal changes can occur very rapidly and can be so severe that their distinction from retrograde changes is either very difficult or impossible.

of M. Rose) and the archicortex (Ammon's formation) receive such projections. In regard to the insular cortex and the pyriform cortex our experiments are inconclusive. Concerning Ammon's formation, although also inconclusive, they suggest that its destruction has no influence on dorsal thalamic elements. (Compare RW 6 in which Ammon's formation was destroyed with RW 8 in which it was preserved.) In all experiments in which Ammon's formation was removed changes were observed in at least some septal nuclei[5] and in area diagonalis. On the other hand in 2 animals in which Ammon's formation and fornix were entirely spared (RW 8, RW 30) no conspicuous changes were found either in the septum or in the diagonal area regardless of whether striatum and amygdala were intact (RW 8) or largely destroyed (RW 30). It should be pointed out, however, that in both these animals the olfactory structures in front of the septum were practically entirely preserved, whereas in all other animals they were completely or nearly completely destroyed. Moreover, in RW 30 the oroventral part of the striatum was preserved.

The changes in single septal nuclei and in area diagonalis will not be described here because this does not lie within the scope of the present paper and because the data do not yet permit a detailed analysis. However, two noteworthy facts may be mentioned. The first is that the medial septal nucleus, at least, degenerates completely after removal of the rest of the telencephalon, the second, that it is possible experimentally to split the septal group of nuclei. The behavior of the medial septal nucleus (and possibly other septal structures) is especially important because this provides experimental evidence that it is noncortical in nature. According to the classical study of Nissl (1911) an acute and complete degeneration does not occur in any cortical area even if all its connections are destroyed. It is tempting to use this criterion for those telencephalic structures in regard to which it is not simple to say on the basis of structure whether they are cortex or not. In this connection it is interesting that taenia tecta, for which there is comparative anatomical evidence suggesting that it is cortex, and all other structures which we regard as cortical areas really behaved as cortex in all our experiments.

[5] For definition of septal nuclei see footnote on p. 70.

### *C. The ventral thalamus*

In contrast with the epithalamus and the dorsal thalamus, the ventral thalamus does not behave uniformly after ablation of the telencephalon. The reticular complex degenerates severely, the suprahypothalamic group shows questionable changes and no demonstrable alterations occur in the ventral lateral geniculate body. The latter fuses early in ontogeny with the subthalamus of our demarcation (suprapenduncular complex or zona incerta and corpus subthalamicum) and it may belong to this group functionally. However, in total ablation experiments some changes were observed in the suprapeduncular complex and severe changes occurred in corpus subthalamicum and in substantia nigra.[6]

With respect to the reticular complex, it is important to point out that despite its degeneration after removal of the whole telencephalon, it differs essentially from all dorsal thalamic elements. The fact, that the reticular complex arises from a totally different area than does the dorsal thalamus, suggests that functionally the two are different. In fact, it was pointed out by Nissl (1913) that the reticular complex, though clearly demarcated (Figs. 14–20), does not behave as a unit after circumscribed lesions of the cortex. He found that, in addition to degeneration of the dorsal thalamic element dependent on the area destroyed, localized lesions always caused degeneration of a certain sector of the reticular complex, differing according to the location of the cortical ablation. This nucleus, therefore, seems to project to the cortex in a different manner than do other single elements, and it cannot be brought to complete degeneration unless the whole cortex is removed. At present, we have a number of rabbit brains with circumscribed large and small lesions in different parts of the cortex, which show that localized changes in the reticular complex can be produced from various regions of the cortex. Whether they can be produced from every cortical field we do not yet know. It is clear, however, that the projection area of the reticular complex must be very extensive.

If this concept of the reticular complex is correct, one must consider

[6] Changes in the subthalamus and substantia nigra were conspicuously absent when subcortical centers were preserved (RW 6 and RW 8). These changes will be reported elsewhere but it may be said that our experiments so far are in essential agreement with the findings of Ferraro (1924).

two types of projection system from the thalamus, one from the nuclei of the dorsal thalamus projecting to circumscribed cortical fields, a second from the ventral thalamus projecting to the whole cortex or to extensive portions of it.[7] If this is so, the reticular complex cannot be compared to any single element of the dorsal thalamus, but rather, perhaps, to the whole projection system of the dorsal thalamus. This conception is harmonious not only with the ontogenetic origin of the reticular complex but also with its unique topographical situation and with the variations in its cellular composition in its various sectors. It is obvious that, after removal of the whole telencephalon, the differences in behavior of the reticular complex and the dorsal thalamus cannot be distinguished. The cells of the reticular complex, however, seem to be much more resistant to degeneration than any cells of the dorsal thalamus except, perhaps, those in some sectors of the anterodorsal nucleus. As has been pointed out, many cells in the reticular complex show little change 19 days after total ablation of the telencephalon and not before 4 weeks are severe changes present in most cells. Even then many neurons are still visible in this complex.

Whether or not the reticular complex has prominent subcortical connections cannot be answered by the present experiments, because none of our animals with subcortical telencephalic centers intact lived longer than 19 days. For this reason it is not justifiable to assume that the excellent preservation of many cells in this complex is due to incomplete removal of the projection area. Likewise, we hold that Waller's (1938) statement, regarding the presence of subcortical connections for this complex in the cat, is inconclusive.

## SUMMARY

Evidence has been presented to show that:

1. The epithalamus (*i.e.*, the paraventricular complex, the habenular complex and the pretectal group) remains unchanged after ablation

[7] Recently, Morison and Dempsey (1942) have secured physiological evidence which has led them to postulate the existence of 2 types of projection system from the thalamus to the cortex. The first of these is the well known specific projection system with more or less point to point arrangement; the second is "non-specific" with diffuse connections. It is evident that the reticular complex fulfills the anatomical requirements of such a diffuse system. However, these authors obtained their diffuse (the "recruiting") response mainly on electrical stimulation of the intralaminar group of nuclei.

of the cortex and, in fact, is independent of the whole telencephalon. Thus, the whole epithalamus behaves uniformly in accord with ontogenetic and phylogenetic considerations.

2. All elements of the dorsal thalamus (midline and intralaminar nuclei included) degenerate entirely after ablation of the telencephalon. After 4 weeks degeneration is practically equally severe in every element and there are no nuclear groups, single nuclei or parts thereof which remain unaffected. In addition, all major dorsal thalamic elements are cortical dependencies. The small group of midline and intralaminar nuclei, for which it was not posible to exclude dependence on striatum and amygdala, can depend on the cortex as well. The possibility that all dorsal thalamic nuclei are dependent only on the cortex is discussed.

3. The ventral thalamus (reticular complex, ventral lateral geniculate body, and the suprahypothalamic group), in contrast with the epithalamus and dorsal thalamus, does not react uniformly after ablation of the telencephalon; only the reticular complex degenerates. The reticular complex projects to the cortex, but whether or not it also projects to subcortical telencephalic centers has not been established. Unlike single elements of the dorsal thalamus, the reticular nucleus projects extensively to the cortex. This is discussed.

We wish to express our deep appreciation to Dr. Adolf Meyer for the hospitality of his laboratory and to thank Miss Cecilia Bisson and Mrs. Thelma Short of the laboratory staff for the preparation of the sections.

The drawings and the lettering of the photographs were done by Mr. P. D. Malone.

## REFERENCES

BARD, P., AND RIOCH, D. MCK.: A study of four cats deprived of neocortex and additional portions of the forebrain. *Bull. Johns Hopkins Hosp.*, 1937, **60:** 73–147.

BODIAN, D.: Studies on the diencephalon of the Virginia opossum. Part III. The thalamo-cortical projection. *J. Comp. Neurol.*, 1942, **77:** 525–575.

BROUWER, B.: Examen anatomique du système nerveux central des deux chats décrits par J. G. Dusser de Barenne. *Arch. Néerl. Physiol.*, 1920, **4:** 124–176.

CLARK, W. E. LEGROS: An experimental study of thalamic connections in the rat. *Philos. Trans.*, 1932, **222: B:** 1–28.

CLARK, W. E. LEGROS, AND BOGGON, R. H.: On the connections of the anterior nucleus of the thalamus. *J. Anat., London*, 1933a, **67:** 215–226.

CLARK, W. E. LEGROS, AND BOGGON, R. H.: On the connections of the medial cell groups of the thalamus. *Brain*, 1933b, **56:** 83–98.

CLARK, W. E. LEGROS, AND RUSSELL, W. R.: Observations on the efferent connexions of the centre median nucleus. *J. Anat., London*, 1939, **73:** 255–262.

FERRARO, A.: *Étude Anatomique du Système Nerveux Central d'un Chien dont le Pallium A Été Enlevé.* (Utrecht, Zuidam) 1924, 101 pp.

FOX, C. A.: Certain basal telencephalic centers in the cat. *J. Comp. Neurol.*, 1940, **72:** 1–62.

INGRAM, W. R., HANNETT, F. I., AND RANSON, S. W.: The topography of the nuclei of the diencephalon of the cat. *J. Comp. Neurol.*, 1932, **55:** 333–394.

KAPPERS, C. U. A., HUBER, G. C., AND CROSBY, E. C.: *The Comparative Anatomy of the Nervous System of Vertebrates, Including Man.* (New York, Macmillan) 1936, 2 vols.

LASHLEY, K. S.: Thalamo-cortical connections of the rat's brain. *J. Comp. Neurol.*, 1941, **75:** 67–121.

MONAKOW, C. VON: Experimentell- und pathologisch-anatomische, sowie entwicklungsgeschichtliche Untersuchungen über die Beziehungen des Corpus striatum und des Linsenkernes zu den übrigen Hirnteilen. *Schweiz. Arch. Neurol. Psychiat.*, 1925, **16:** 225–234.

MORISON, R. S., AND DEMPSEY, E. W.: A study of thalamo-cortical relations. *Amer. J. Physiol.*, 1942, **135:** 281–292.

MORRISON, L. R.: *Anatomical Studies on the Central Nervous Systems of Dogs without Forebrain or Cerebellum.* (Haarlem, De Erven F. Bohn) 1928, viii, 109 pp.

MÜNZER, E., UND WIENER, H.: Das Zwischen- und Mittelhirn des Kaninchens und die Beziehungen dieser Teile zum übrigen Centralnervensystem, mit besonderer Berücksichtigung der Pyramidenbahn und Schleife. *Mschr. Psychiat. Neurol.*, 1902, **12:** 241–279.

NISSL, F.: Zur Lehre der Lokalisation in der Grosshirnrinde des Kaninchens. I. Teil. Völlige Isolierung der Hirnrinde beim neugeborenen Tiere. *S. B. Heidelb. Akad. Wiss.*, 1911, **38 Abh.:** 1–70.

NISSL, F.: Die Grosshirnanteile des Kaninchens. *Arch. Psychiat. Nervenkr.* 1913, **52:** 867–953.

PAPEZ, J. W.: Thalamic connections in a hemidecorticate dog. *J. Comp. Neurol.*, 1938, **69:** 103–120.

PAPEZ, J. W., AND FREEMAN, G. L.: Superior colliculi and their fiber connections in the rat. *J. Comp. Neurol.*, 1930, **51:** 409–439.

RIOCH, D. MCK.: A note on the centre médian nucleus of Luys. *J. Anat., London*, 1931, **65:** 324–327.

ROSE, J. E.: The ontogenetic development of the rabbit's diencephalon. *J. Comp. Neurol.*, 1942a, **77:** 61–129.

ROSE, J. E.: The thalamus of the sheep: cellular and fibrous structure and comparison with pig, rabbit and cat. *J. Comp. Neurol.* 1942b, **77:** 469–523.

ROSE, M.: Über das histogenetische Prinzip der Einteilung der Grosshirnrinde. *J. Psychol. Neurol., Lpz.*, 1926, **32:** 97–160.

ROSE, M.: Cytoarchitektonischer Atlas der Grosshirnrinde des Kaninchens. *J. Psychol. Neurol., Lpz.*, 1931, **43:** 353–440.

ROSE, M.: Das Zwischenhirn des Kaninchens. *Mém. Acad. Pol. Sc. Lett.* 1935, **B:** 1–108.

ROTHMANN, H.: Zusammenfassender Bericht über den Rothmannschen grosshirnlosen Hund nach klinischer und anatomischer Untersuchung. *Z. ges. Neurol. Psychiat.*, 1923, **87:** 247–313.

STOFFELS, J.: Organisation du thalamus et du cortex cérébral chez le lapin. *J. Belge Neurol. Psychiat.*, 1939a, **39:** 557–575.

STOFFELS, J.: La projection de noyaux antérieurs du thalamus sur l'écorce interhémisphérique. *J. Belge Neurol. Psychiat.*, 1939b, **39:** 743–776; 783–833.

SCHALTENBRAND, G., AND COBB, S.: Clinical and anatomical studies on two cats without neocortex. *Brain*, 1931, **53:** 449–488.

WALKER, A. E.: The thalamus of the chimpanzee. II. Its nuclear structure, normal and following hemidecortication. *J. Comp. Neurol.*, 1938a, **69:** 487–507.

WALKER, A. E.: *The Primate Thalamus.* (Chicago, Univ. Chicago Press) 1938b, xxiv, 321 pp.

WALLER, W. H.: Topographical relations of cortical lesions to thalamic nuclei in the albino rat. *J. Comp. Neurol.*, 1934, **60:** 237–269.

WALLER, W. H.: A cortical lesion causing cell reaction in the anteromedial thalamic nucleus. *J. Comp. Neurol.*, 1937, **66:** 443–448.

WALLER, W. H.: The thalamus of the cat after hemidecortication. *J. Anat., London*, 1938, **72:** 475–487.

WALLER, W. H.: Thalamic connections of the frontal cortex of the cat. *J. Comp. Neurol.*, 1940, **73:** 117–138.

WINKLER, C., AND POTTER, A.: *An Anatomical Guide to Experimental Researches on the Rabbit's Brain.* (Amsterdam, W. Versluys) 1911. (WINKLER, C.: *Opera omnia, T. suppl.*, 1)

YOUNG, M. W.: The nuclear pattern and fiber connections of the non-cortical centers of the telencephalon of the rabbit (*Lepus cuniculus*). *J. Comp. Neurol.*, 1936, **65:** 295–401.

# THE FLUORESCEIN TEST IN THE MANAGEMENT OF TUBED (PEDICLE) FLAPS

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Received for publication May 27, 1943

For the plastic surgeon, pedunculated flaps are of unique value in the restoration of function and reconstruction of parts of the body where loss of skin and subcutaneous tissue has occurred. Of the several types of pedunculated flaps, the tubed flap is frequently employed for a wide variety of reconstructive procedures (1). One of the problems in the management of tubed flaps is the estimation of the circulation and determination of the time at which transfer of one of the pedicles may be safely accomplished. Davis (1) states that "the question often arises as to when the circulation of delayed transfer skin flaps will be sufficiently developed to allow the division of the first pedicle so that the circulation from the other pedicle will be adequate to nourish the flap without loss of tissue. There is a wide divergence of opinion on this subject, different authors advising that from several weeks to as many months be allowed to elapse before dividing one pedicle and making the transfer. The time usually advised is about 3 weeks." Davis adds that "after the transfer of a tubed flap the new circulation may be tested by a stomach clamp across the pedicle sufficiently tight to block the circulation . . . ."

We wish to describe a method for the exact estimation of the circulation in tubed flaps which is based on the technique described by Lange and Boyd (2) in which sodium fluorescein is injected intravenously and the part in question observed under ultraviolet light.

## METHOD

Sixteen healthy mongrel dogs of both sexes were operated upon under anesthesia induced by intravenous soluble pentobarbital, and double pedicled tubed flaps of various lengths were formed on either side of the midline of the back. After intervals of 2 to 7 weeks one of the pedicles of the tubed flaps was transferred to another site on the back and sutured to the skin edges of a freshly made defect. At successive stages the opposite pedicles were reimplanted at intervals of 7–25 days

following the original transfer. 10 cc. of a 20 per cent solution of sodium fluorescein was administered intravenously before each operation and usually on several occasions after each transfer. A rubber-shod stomach clamp was applied to the "old" pedicle immediately prior to injection in order to determine the circulation through the transferred end. The clamp was left in place for no longer than 5 minutes after which time no further information was obtainable.

Plaster collars were applied to each animal's neck at the original operation in order to prevent biting of the tube.

## RESULTS

Under ultraviolet light the shaved skin of the dog's back and of the tubed flap is purple, but following the injection of sodium fluorescein the entire area becomes a bright yellow-green with the exception of scar tissue which remains purple.[1] This change begins in 15 to 20 seconds and is noted wherever the blood circulates. By this technique it is not only possible to determine whether blood circulates through a given point but also the relative amount reaching that area for different intensities of yellowish-green are easily distinguishable.

The following facts were established: That in no case did gangrene or slough occur following a transfer of one of the pedicles if the fluorescein test had shown the pedicle to receive blood from the other end. In 2 dogs complete vascularization had occurred by the 7th day and transfer was successful. One week later the fluorescein test again showed an adequate blood supply of the tubed flap from the new pedicle and following division of the old pedicle viability of the entire tube and pedicle of each dog confirmed the accuracy of the test. On the other hand, 3 tubed flaps were transferred when the flourescein test had shown only 50 per cent or less of the tube to have circulation from the new pedicle. In 2 out of these 3 cases gangrene of the pedicle occurred. However, the slough did not extend as far back as the line of demarcation indicated by fluorescein. This observation would seem to be of value by showing that there was some circulation beyond the point observed by the test, thus indicating that a margin of safety exists.

We have applied the test to three patients with tubed flaps and have confirmed the experimental findings. Two of these flaps have been

[1] The reader is referred to LIFE MAGAZINE, Vol. 13, No. 22, Nov. 30th, 1942 for photographs illustrating the color changes characteristic of fluorescein under ultraviolet light.

transferred with successful takes while operation is planned for the third patient in the near future.

Two points are worth noting: That 10 cc. of the sodium fluorescein in man makes the color change more readily distinguishable than a smaller amount of the drug; the only untoward symptom noted either in man or dog was a transient nausea which seemed to be related to the speed of the injection, slow injection (1 minute for 10 cc.) usually having caused no nausea.

## SUMMARY

Tubed flaps were fashioned in dogs and studied both before and after several transfers of the pedicles by means of the fluorescein test.

1. The test proved to be an accurate indication of the integrity of the circulation. Whenever a discrepancy existed between the actual circulation as determined by subsequent operative procedure and the fluorescein test, the difference lay in a factor of safety for the test.
2. Clinical trial of the fluorescein test in three patients with tubed flaps confirmed the experimental observations.

## CONCLUSIONS

By means of the fluorescein test the earliest possible time for transfer of a tubed flap can be determined and the transfer of a pedicle carried out with assurance that the circulation is adequate. The test is simple to perform and apparently safe in the dosage necessary for accurate determination of color changes. Although we have not performed the test on children it would seem advisable to use correspondingly smaller doses.

## BIBLIOGRAPHY

1. Davis, J. S.: *Practice of Surgery*, Dean Lewis, Editor, W. F. Prior Co., Hagerstown, Md. Vol. 5, Chapter 8, page 68.
2. Lange, K., and Boyd, L. J.: The Use of Fluorescein to Determine the Adequacy of the Circulation, *M. Clin. North America*, **26**: 943, 1942.

# VITAMIN A LEVELS IN MATERNAL AND FETAL BLOOD PLASMA[1]

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Received for publication June 12, 1943

Vitamin A was determined in the blood plasma of 297 women at term and in 14 women at various intervals during the course of pregnancy. In 50 cases the vitamin A level of the fetal cord blood was also obtained. The determinations were made on samples of oxalated blood plasma by the alcohol precipitation method recommended by Yudkin (1) and adapted to the Klett colorimeter. Dilutions of U.S.P. reference cod liver oil in chloroform and of beta-carotene in petroleum ether were used to plot the standard reference curves.

## VITAMIN A LEVELS IN PREGNANCY

The group of 247 women who were studied at term included 157 white patients and 137 colored patients. The average level was 118 International Units of vitamin A per 100 ml. of plasma. The level of of 112 I.U. for colored patients was slightly lower than that for white patients which was 123 I.U. (Table I).

In only 14 cases (5 per cent) were the levels of vitamin A below 50 I.U. per 100 ml. plasma. Although this group included various types of obstetrical conditions the incidence of obstetrical complications among them was no higher than among patients with higher vitamin A levels. No correlation between A levels and such clinical phenomena as puerperal infection, abortion, premature labor, toxemia or hemorrhage could be found. The proportion of mothers who were able to nurse their infants was approximately the same at all levels of vitamin A. Six patients received mineral oil during pregnancy. The carotene and vitamin A levels were apparently not lowered by such medication.

A study of family income showed that there was no difference in the average vitamin A level in women belonging to families whose income was less than $2.00 per person per week and those in higher income brackets (Table II).

[1] This study was supported in part by a bequest from the estate of Mrs. Lucy Wortham James.

Although the survey revealed no significant lowering of plasma vitamin A at term, the level was somewhat below that observed in a similar economic and social group of non-pregnant healthy women. Fifty normal women had an average level of 134 I.U. per 100 ml. The aver-

TABLE I

| No. Cases | Average Vit. A/100 ml. |
|---|---|
| Pregnant women at term | |
| | *I.U.* |
| 157 white | 123 |
| 137 colored | 112 |
| 294 total | 118 |
| Non-pregnant women | |
| 25 white | 146 |
| 25 colored | 123 |
| 50 total | 134 |

TABLE II

*Economic data*

| INCOME PER PERSON IN FAMILY PER WEEK | WHITE | | COLORED | |
|---|---|---|---|---|
| | No. cases | Vit. A/100 ml. | No. cases | Vit. A/100 ml. |
| *dollars* | | *I.U.* | | *I.U.* |
| 0–2 | 3 | 109 | 12 | 113 |
| 2–4 | 13 | 109 | 36 | 112 |
| 4–6 | 13 | 140 | 25 | 116 |
| 6–8 | 10 | 105 | 16 | 138 |
| 8–10 | 21 | 112 | 20 | 88 |
| 10–12 | 15 | 140 | 5 | 108 |
| 12–14 | 16 | 105 | 5 | 126 |
| 14–16 | 17 | 146 | | |
| over 16 | 28 | 123 | | |

age for white women was 146 I.U. and for colored 123 I.U. (Table I). The lower figures for the pregnant women may be due to the increased nutritional demands of pregnancy, or may be a result of the blood dilution which is present at term.

Fourteen patients were studied at intervals during the prenatal

period. Throughout the course of pregnancy the average vitamin A levels deviated only slightly from the average value of 118 I.U. found in the larger series at term, although wide fluctuations occurred in many individuals (Table III). Post partum values promptly showed a tendency to return to the average non-pregnant levels.

### VITAMIN A LEVELS IN FETAL BLOOD PLASMA

In the past there have been several reports which would indicate that fetal or cord blood contains only traces of vitamin A and carotene, and that the liver storage is low. Wolff (2) in 1932 reported that newborn infants had very little vitamin A stored in the liver. Menken

TABLE III

*Prenatal vitamin A in 14 cases*

| WEEKS | NUMBER OF DETERMINATIONS | AVERAGE VIT. A/100 ML. |
|---|---|---|
| | | *I.U.* |
| 1– 8 | 2 | 116 |
| 9–12 | 9 | 109 |
| 13–16 | 8 | 118 |
| 17–20 | 13 | 115 |
| 21–24 | 11 | 132 |
| 25–28 | 12 | 108 |
| 29–32 | 19 | 111 |
| 33–36 | 18 | 122 |
| 37–40 | 15 | 120 |
| Term | 5 | 117 |
| Postpartum | 11 | 139 |

(3) found that of 76 infants studied, 48.7 per cent had no detectable vitamin A in their cord blood, and similarly Gaehtgens (4) reported that in a group of 26 samples of cord blood only one showed a trace of vitamin A. Clausen and McCoord (5) detected substantial amounts of carotene and vitamin A in fetal blood but were of the opinion that the values were not high enough to suggest ready transfer of vitamin A across the placental barrier.

In the present experiment determinations were made on the cord blood of fifty infants. All showed substantial amounts of vitamin A in the plasma. The average value was 91.3 I.U. per 100 ml. and the corresponding average maternal level, taken a few hours before delivery, was 106.3 I.U. Although the average values in maternal

and fetal blood plasma were close to one another, individual cases showed no constant relationship (Table IV). In ten cases the fetal level was far above the maternal, in 21 cases it was within 25 I.U. of the maternal and in 19 cases it was more than 25 I.U. below the maternal level. In the entire group of 50 cases only 11 showed a fetal level below 70 I.U. per 100 ml. plasma indicating that the fetus has substantial amounts of vitamin A in the circulating blood. Wide differences between fetal and maternal values could not be correlated with toxemias, premature labor, twins or other obstetrical complications.

No carotene could be detected in 28 of the 3 ml. samples used in the determination. The remaining 22 cases showed traces of carotene, but the average for the 50 cases was only 2.01 micrograms per 100 ml. whereas the maternal average was 106.3 micrograms per 100 ml.

From these results it seemed probable to us that vitamin A per se is the substance which crosses the placental barrier. Therefore feeding experiments were carried out in an effort to raise significantly the fetal vitamin A level. The feeding technic was based on the observations of Murril et al. (6) and Ralli, Bauman and Roberts (7).

Fifteen women in labor were fed vitamin A capsules every two hours until delivery. Some received as much as 200,000 I.U. during a period of 8 hours. The vitamin A in the maternal blood usually rose sharply, two cases attaining levels of over 400 I.U. per 100 ml. at the time of delivery. In no instance however, was it possible to raise the vitamin A level of the infant above the values obtained in untreated cases. Usually it did not rise above the initial maternal level, determined before vitamin therapy was instituted.

Three additional women received 100,000 I.U. of vitamin A orally every day for several days preceding delivery. However, even by this technic it was not possible to raise the vitamin A to significant heights.

In order to study the role of carotene, three patients were fed $\beta$-carotene in peanut oil for several days before delivery. They received an initial dose of 100 mg. the first day and 50 or 100 mg. every three days thereafter until delivery. The maternal carotene level was maintained at 130 micrograms or more per 100 ml. and during this period there was usually a gradual rise in the vitamin A level. However, the infant cord blood in each case showed vitamin A and carotene values which were well within the normal untreated range.

TABLE IV

*Vitamin A and carotene levels in fetal and maternal blood per 100 ml. of plasma*

| CASE NO. | RACE | I. U. VITAMIN A | | | MICROGRAMS OF CAROTENE | |
|---|---|---|---|---|---|---|
| | | Fetal | Maternal | Diff. | Fetal | Maternal |
| 59 | C | 167 | 85 | +82 | 10 | 141.2 |
| 84 | W | 130 | 53 | +77 | 0.0 | 100 |
| 61 | C | 129 | 53 | +76 | 6.6 | 100 |
| 27 | W | 131 | 66 | +65 | 0.0 | 90 |
| 3 | W | 122 | 68 | +54 | 10 | 93.3 |
| 23 | W | 136 | 85 | +51 | 6.6 | 46.3 |
| 32 | C | 109 | 64 | +45 | 6.6 | 48.2 |
| 88 | W | 129 | 88 | +41 | 2.3 | 100 |
| 104 | W | 124 | 95 | +29 | 0.0 | 102 |
| 108 | W | 99 | 71 | +28 | 6.0 | 86.6 |
| 105 | C | 55 | 36 | +19 | 0.0 | 90 |
| 13 | C | 108 | 89 | +19 | 2.3 | 76 |
| 58 | C | 72 | 58 | +14 | 2.3 | 235 |
| 14 | C | 100 | 86 | +14 | 1.3 | 60 |
| 78 | W | 122 | 115 | +7 | 0.0 | 101.3 |
| 5 | W | 53 | 48 | +5 | 0.0 | 70 |
| 67 | C | 78 | 73 | +5 | 0.0 | |
| 86 | W | 130 | 128 | +2 | 0.0 | 83 |
| 53 | C | 70 | 70 | 0 | 6.6 | 230 |
| 80 | W | 60 | 61 | −1 | 0.0 | 60 |
| 82 | C | 120 | 121 | −1 | 0.0 | 86.6 |
| 17 | C | 128 | 130 | −2 | 8.0 | 116.6 |
| 26 | W | 47 | 50 | −3 | 2.6 | 116.6 |
| 24 | W | 139 | 144 | −5 | 10 | 190 |
| 63 | W | 120 | 125 | −5 | 0.0 | 96.6 |
| 29 | W | 83 | 91 | −8 | 2.0 | 116.6 |
| 107 | W | 98 | 109 | −11 | 2.0 | 106.6 |
| 68 | C | 78 | 91 | −13 | 3.3 | 106.6 |
| 60 | C | 113 | 130 | −17 | 0.0 | 46.6 |
| 12 | C | 81 | 100 | −19 | 3.3 | 66.6 |
| 71 | C | 100 | 122 | −22 | 2.0 | 118.3 |
| 69 | W | 81 | 110 | −29 | 3.3 | 91.6 |
| 77 | C | 103 | 146 | −43 | 0.0 | 53.3 |
| 40 | W | 78 | 123 | −45 | 0.0 | 76.6 |
| 92 | C | 73 | 112 | −49 | 0.0 | 103.3 |
| 21 | W | 149 | 198 | −49 | 6.6 | 96.6 |
| 41 | W | 78 | 135 | −57 | 0.0 | 50 |
| 11 | W | 46 | 105 | −59 | 0.0 | 33.3 |
| 74 | C | 90 | 140 | −60 | 0.0 | 100 |
| 70 | C | 30 | 101 | −71 | 0.0 | 100 |
| 16 | C | 300 | 102 | −72 | 0.0 | 110 |
| 28 | W | 90 | 163 | −73 | 0.0 | 113.3 |
| 65 | W | 96 | 174 | −78 | 0.0 | 73.3 |
| 81 | W | 47 | 125 | −78 | 0.0 | 76.6 |
| 22 | W | 66 | 147 | −81 | 13.0 | 126.6 |
| 73 | W | 75 | 156 | −81 | 0.0 | 100 |
| 64 | W | 83 | 170 | −87 | 0.0 | 33.3 |
| 83 | W | 47 | 138 | −91 | 0.0 | 91.6 |
| 20 | C | 36 | 129 | −93 | 0.0 | 100 |
| 18 | C | 40 | 136 | −96 | 0.0 | 16.6 |

From these results it must be concluded that the transfer of vitamin A and/or carotene across the placenta cannot be detected by the feeding methods employed in this experiment. However, the constant presence of substantial amounts of vitamin A in the fetal blood would suggest that the infant needs and utilizes vitamin A during fetal life. The source of the vitamin, whether by direct passage of vitamin A from the mother, or by synthesis from transferred carotene has not been elucidated. It may be that the vitamin A gradually stored in the fetal liver has an influence on the level in the fetal circulation. Thus the vitamin A level in cord blood would be an indication of the liver storage level rather than a value closely correlated with fluctuations in the maternal blood vitamin A.

## SUMMARY AND CONCLUSIONS

Provided the plasma vitamin A levels can be regarded as an index of nutritional status in regard to vitamin A, the present findings do not indicate that vitamin A depletion is a common cause of obstetrical complication among metropolitan dispensary groups.

There are substantial amounts of vitamin A and traces of carotene in fetal plasma. The fetal values, however, cannot be raised by increasing the maternal vitamin A or carotene levels. The problem of placental transfer of vitamin A is still unclear.

## REFERENCES

1. YUDKIN, S., Estimation of Carotene and Vitamin A in Human Blood. *Biochem. J.*, **35:** 551, 1941.
2. WOLFF, L. K., On the Quantity of Vitamin A Present in Human Liver. *The Lancet*, **2:** 617, 1932.
3. MENKEN, J. G., Vitamin A and Carotinoid Content of Human Serum and Milk. *Nutritional Abst. and Rev.* **5:** 57, 1935.
4. GAEHTGENS, G., Bestimmungen von Carotin und Vitamin A im Nabelschneurblut. *Klin. Wchnschr.*, **16:** 894, 1937.
5. CLAUSEN, S. W., AND MCCOORD, A. B., The Carotinoids and Vitamin A of the Blood. *J. Pediat.* **13:** 635, 1938.
6. MURRIL, W. A., HORTON, P. B., LIEBERMAN, E., AND NEWBURGH, L. H., Vitamin A and Carotene Metabolism in Diabetics and Normals. *J. Clin. Invest.*, **20:** 395, 1941.
7. RALLI, E. P., BAUMAN, E., AND ROBERTS, L. B., The Plasma Levels of Vitamin A after Ingestion of Standard Doses. Studies of Normal Subjects and Patients with Cirrhosis of the Liver *J. Clin. Invest.*, **20:** 709, 1947.

# DEFORMOL

## A Simple Technique for Removing Formaldehyde from Preserved Tissue Specimens

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Received for publication May 12, 1943

In practically all laboratories and teaching institutions gross histological and pathological tissue specimens are placed in chemical solutions for fixation and preservation until such time as they may be required for further examination and study. Most of the fixative solutions employed contain varying amounts of mercuric chloride, bichromates, picric acid, potassium acetate, etc. with from three to ten per cent of formaldehyde.

Students and instructors who frequently work with such material over prolonged periods of time are exposed to the disagreeable fumes of the formaldehyde which are not only unpleasant but hazardous. This gas is irritating to the eyes and respiratory tract, producing bronchitis and predisposing the worker to the common cold, and in addition may also produce a severe local dermatitis.

During the past years the writer has attempted to develop a formula for removing the formaldehyde from preserved specimens, and a number of chemicals known to react with formalin have been tried with some degree of success. Solutions containing potassium and sodium bisulfite were found to be effective but in combining with the reducing aldehyde and formic acid free sulphur dioxide gas was formed in sufficient quantity to preclude their general use.

The use of ammonia water to reduce the irritating effects of formaldehyde is generally known. Usually the specimen is immersed for a brief period in a solution of fifteen to twenty cubic centimeters of ammonium hydroxide to each liter of water. While this reduces the amount or effect of the formaldehyde to some extent it is also irritating to the eyes and nasal passages.

Foust *et al.* (1) reported on the use of a solution of urea and ammonium phosphate and later Fort *et al.* (2) described a sulfite-bisulfite solution used in removing formalin from preserved specimens.

We have found the following formula to be effective, rapid in action and non-irritating in the form and strength used. The reagents are readily available to any laboratory and so inexpensive that the solution may be used in generous quantities and discarded after use.

| | |
|---|---|
| Sodium thiosulfate | 120 gms. |
| Ammonium hydroxide—28 per cent | 5 cc. |
| Glycerin | 75 cc. |
| Water, sufficient to make up | 1000 cc. |

In class room or other group work, solutions of this type may be used in considerable quantities and will be less expensive if the commercial or the U.S.P. grade of chemicals is used. The slight variations in quality of the commercial "Hypo" (sodium thiosulfate) will not materially reduce the effectiveness of the formula. The solution should remain slightly on the alkaline side, and if kept in large stock bottles a few drops of one-tenth per cent alcoholic Thymol Blue may be added until a faint blue color is imparted to the solution. If this color disappears on standing it will indicate that the pH has dropped below pH 8.0 and small amounts of ammonium hydroxide should be added until the blue color is restored.

Specimens removed from the formaldehyde fixing solution should be first rinsed in tap water, and then placed in a container with a sufficient quantity of the deformalinizing solution to cover the entire specimen. Specimens weighing from two to three hundred grams will be practically free of formalin odor in three minutes. Larger specimens, especially those containing cavities filled with the fixative may require an additional short immersion in the thiosulfate solution after being sectioned. Deformalinization is here due to the reaction between the sodium thiosulfate and the formaldehyde and the conversion of free formic acid into ammonium formate. The glycerin serves to prevent rapid drying of surface areas.

Small blocks of tissue were allowed to remain in the deformalinizing bath for twelve hours, after which they were sectioned and stained for microscopic study in the usual manner. The staining characteristics of the cellular nuclei of this tissue appeared to be slightly weaker than those of the control blocks sectioned at the same time, but tissue blocks which were allowed to remain in deformalinizing solution for eight hours or less showed no appreciable change.

While gross specimens will not be impaired if allowed to remain in this bath for several days it must not be regarded as a substitute for the various preservative solutions now in general use. If dissection or other study requires that the specimen be handled for several successive days we suggest that it be rinsed in tap water and returned to the preservative at the end of each day.

## REFERENCES

1. Foust, H. F., *Science*, **83:** 498, 1935.
2. Fort, W. B., *Science*, **94:** 168, 1941.

## BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this Journal.)

*Blood Grouping Technic.* By FRITZ SCHIFF and WILLIAM C. BOYD. 248 pp. Illus. $5.00. Interscience Publishers, New York, 1942.

Dr. Schiff's posthumous book is a neatly presented monograph on the whole field of blood groups. It is a readable, well organized book, and the descriptions of techniques are admirably specific and clear. Every phase of blood groups,medical, medico-legal, anthropological is covered. New developments receive adequate and lucid exposition. For the clarity of the discussions and the detailed simplicity of the descriptions of technical procedures this reviewer prefers Dr. Schiff's book to the few others available in English.

M. M. R.

*The Blood Bank and the Technique and Therapeutics of Transfusions.* By ROBERT A. KILDUFFE and MICHAEL DEBAKEY. 558 pp. Illus. $7.50. C. V. Mosby Company, St. Louis, 1942.

For years systems and text books of medicine and surgery have presented consistently inadequate descriptions of outmoded methods of transfusion. The few books dealing with blood transfusion in the past have concerned themselves more particularly with the minutiae of blood grouping and have had little practical information for the clinician. The present work, coming at a time of great interest in the subject, admirably satisfies the need for a comprehensive discussion of blood transfusion. There is a good historical section and adequate discussion of blood groups. The technique of blood transfusion and of the organization of blood banks is discussed in great detail, with practically every recent publication of any value quoted at length. Most of the original accompanying illustrations have been reproduced. The presentation is complete, rather than critical. The same treatment has been accorded the preparation and use of plasma. Most of the fundamental articles are abstracted and their illustrations reproduced.

All in all the book is ideal for those interested in blood transfusions and blood banking and, for those in process of organizing blood banks, presents a wide variety of techniques from which to choose.

M. M. R.

*Standard Nursing Procedures of the Department of Hospitals, City of New York.* Prepared by the Committee on Nursing Standards, Division of Nursing, Department of Hospitals. 436 pp. Illus. $3.25. The Macmillan Company, New York, 1943.

As the title indicates, this book is intended primarily for the use of student and graduate nurses in the institutions controlled by the Department of Hospitals of

the City of New York. It contains material not usually included in a nursing manual. One chapter tells how New York City's public hospital system began, how it has developed and what it hopes to become; another presents the philosophy of nursing as applied to the care of the indigent sick in public institutions. A chapter on "Ward Administration" aims to acquaint members of the nursing staff with the responsibilities of persons in various positions; one on "The Hospital in the Community" stresses the preventive function of hospitals and the responsibility which the nurse has for health teaching.

The major portion of the book is devoted to nursing procedures which are basic to the general care of patients. Wherever special adaptation is required to make a procedure suitable for a child, instructions are given immediately following the general procedure. The sections covering obstetric, pediatric, and neurologic nursing are brief, since they include only those procedures which belong exclusively to these specialities. Frequent references are made to the basic general procedures to avoid repetition and stress the fact that nursing care on all services has many points in common.

Throughout the volume every effort has been made to emphasize that any plan for nursing care must comprehend the whole patient and that the need for adaptation to the individual is constant in effective nursing.

Items of nursing care are presented in logical order; there is uniform arrangement of material; procedures are clearly and concisely outlined; there is a good index, and there are a few good line drawings.

Any nursing manual has limited value outside of the institution for which it is intended, but nurses interested in comparing their techniques with those in other institutions, or in compiling a nursing manual, should find this book interesting and helpful. It is unfortunate that there is not more documentation to authenticate the fact that methods have been based upon sound principles.

V. B.

*Understand Your Ulcer: A Manual for the Ulcer Patient.* By BURRILL B. CROHN. 199 pp. Illus. $2.50. The Sheridan House, Inc., New York, 1943.

This is a book for the patient with peptic ulcer. Its author is one of the leaders of American gastro-enterology. Burrill Crohn is known for his excellent text, "Affections of the Stomach," his numerous contributions to current scientific medical literature, and more recently for his work on regional ileitis, a disease which sometimes bears his name. He comes to this task obviously well equipped.

There are 15 chapters. These deal with such questions as, "What is an Ulcer?," "What Causes an Ulcer?", "Who has Ulcers?", "The X-ray Examination of the Patient and Its Importance", symptoms and complications of ulcer, the diet and medication, immediate and late results of medical management and the indications for and nature of surgical treatment. There are nineteen appropriate illustrations. Sylvia Bayard has contributed a valuable appendix on diet with menus and recipes, and Walter Alvarez has written the preface.

The patient is apprised of the seriousness of the disease without alarming him.

He is given essential information clearly, simply, concisely, completely, and at the same time is made to understand the necessity of competent medical observation and care. The job is well done. This book is recommended not only to the patient for whom it is intended, but also to his physician, who may have need of a good, quick review of this relatively common problem.

M. P.

*Diseases of the Gastro-Intestinal Tract.* By ASHER WINKELSTEIN. 195 pp. $2.00. Oxford University Press, New York (etc.), 1942.

The present state of knowledge of digestive disorders is presented here in truly outline form. Diseases of the oesophagus, diaphragm, stomach, duodenum, gall bladder, pancreas, appendix, small intestine and colon as well as such miscellaneous subject as heart-burn, gastro-intestinal allergy, pellagra and functional diseases of the alimentary tract are taken up. The bibliography consists of the better known text books and monographs in English and in German.

A tremendous amount of information is condensed in a pocket sized book of less than 200 pages. Its value would be enhanced by including liver diseases. Acute transient pancreatitis, newer concepts of disorders produced by the virus of lymphogranuloma venereum as well as of deficiency states other than pellagra in relation to digestive diseases, might well be added in a subsequent edition. However in relation to the whole, these omissions are minor. The outline is really excellent. It has been prepared by a capable teacher and an active contributor to gastro-enterologic medicine. It should fulfill the author's hope both of usefulness to the busy practitioner and as a review source to the student.

M. P.

*Edinburgh Post Graduate Lectures in Medicine.* Vol. II. 540 pp. Illus. 12/6. Published for the Honeyman Gillespie Trust by Oliver and Boyd, Edinburgh and London, 1942.

Post graduate teaching went on in Edinburgh in 1940–41 despite the war. This volume reports some of these activities. It consists of thirty-three lectures. Twenty-seven of the lecturers are of the Edinburgh faculty, the others are from London and Oxford.

The discourses cover an aspect of virtually every field of medicine as is indicated by some of the following titles: On the Contributions of Genetics to Reconstructive Medicine; The Basis of Temperament; The Significance of Fear; Dietetic Treatment of Gastro-Intestinal Disease; Simplification of Blood Examination; Inspection; The Hypertensions; The Surgery of Blood Vessels; Orthopedics—A Brief Survey of its Position; Injuries from Projectiles; Gas Warfare; Pathology of Speech and Voice; Detecting Pelvic Contractions; Care of Children in War Time and After; War and Skin Disease; The Physiological Approach to Medical Problems.

The status of the lecturers gives authoritativeness to this volume.

M. P.